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Bis2A 0.0 Preface to BioStax for Bis2A at UC Davis v1.2

Bis2A is the first quarter of a three quarter series at the University of California, Davis. The purpose of the Bis2 series is really two-fold. First, to provide a broad introduction to all aspects of biology for the biology major and related fields. The second is to prepare our students for the upper division biology core classes consisting of Bis101 (genetics and genomics), Bis102-103 or Bis105 (biochemistry) and Bis104 (cell biology). Bis2A specifically covers the foundations of biology, from atoms to cells. We will be taking a two track approach in this class. The first is from an evolutionary perspective: where did we come from and how did things get so complicated. The second from a "Design Challenge" perspective: How do we build it. The point of this text is to familiarize yourself with the background material. Read the modules, answer the various questions and then be prepared to come to class and discuss your answers and your questions. Text is grounded on an evolutionary basis and includes exciting features that highlight careers in the biological sciences and everyday applications of the concepts at hand. To meet the needs of today's instruction and students, some content has been strategically condensed while maintaining the overall scope and coverage of traditional texts for this course. The text also includes an innovative art program that incorporates critical thinking and clicker questions to help students understand—and apply—key concepts.

Welcome to *Bis2A* and the textbook *Biology*, an OpenStax College resource. This textbook has been created with several goals in mind: accessibility, customization, and student engagement—all while encouraging science students toward high levels of academic scholarship. Instructors and students alike will find that this textbook offers a strong foundation in biology in an accessible format.

About OpenStax College

OpenStax College is a non-profit organization committed to improving student access to quality learning materials. Our free textbooks are developed and peer-reviewed by educators to ensure they are readable, accurate, and meet the scope and sequence requirements of today's college courses. Unlike traditional textbooks, OpenStax College resources live

online and are owned by the community of educators using them. Through our partnerships with companies and foundations committed to reducing costs for students, OpenStax College is working to improve access to higher education for all. OpenStax College is an initiative of Rice University and is made possible through the generous support of several philanthropic foundations.

About OpenStax College's Resources

OpenStax College resources provide quality academic instruction. Three key features set our materials apart from others: they can be customized by instructors for each class, they are a “living” resource that grows online through contributions from science educators, and they are available free or for minimal cost.

Customization

OpenStax College learning resources are designed to be customized for each course. Our textbooks provide a solid foundation on which instructors can build, and our resources are conceived and written with flexibility in mind. Instructors can select the sections most relevant to their curricula and create a textbook that speaks directly to the needs of their classes and student body. Teachers are encouraged to expand on existing examples by adding unique context via geographically localized applications and topical connections.

Biology can be easily customized using our online platform. Simply select the content most relevant to your current semester and create a textbook that speaks directly to the needs of your class. *Biology* is organized as a collection of sections that can be rearranged, modified, and enhanced through localized examples or to incorporate a specific theme of your course. This customization feature will help bring biology to life for your students and will ensure that your textbook truly reflects the goals of your course.

Curation

To broaden access and encourage community curation, *Biology* is “open source” licensed under a Creative Commons Attribution (CC-BY) license. The scientific community is invited to submit examples, emerging research, and other feedback to enhance and strengthen the material and keep it current and relevant for today’s students. Submit your suggestions to info@openstaxcollege.org, and check in on edition status, alternate versions, errata, and news on the StaxDash at <http://openstaxcollege.org>.

A special thanks

I would like to thank the Bis2A Summer Session 1 of 2015 class for their editing comments to these modules. The instructors of Bis2A appreciate all feedback from the students on the reading material.

Cost

Our textbooks are available for free online, and in low-cost print and e-book editions.

About Biology

Biology is designed for multi-semester biology courses for science majors. It is grounded on an evolutionary basis and includes exciting features that highlight careers in the biological sciences and everyday applications of the concepts at hand. To meet the needs of today’s instructors and students, some content has been strategically condensed while maintaining the overall scope and coverage of traditional texts for this course. Instructors can customize the book, adapting it to the approach that works best in their classroom. *Biology* also includes an innovative art program that incorporates critical thinking and clicker questions to help students understand—and apply—key concepts.

Coverage and Scope

Biology meets the scope and sequence of a typical two semester biology course for biology majors, pre-med majors, and science majors. In developing *Biology*, we listened to hundreds of General Biology instructors who readily provided feedback about their courses, students, challenges, and hopes for innovation. The expense of textbooks and related items did prove to be a barrier to learning. But more importantly, these teachers suggested improvements for the textbook, which would ultimately lead to more meaningful and memorable learning experiences for students.

The result is a book that addresses a core organizational reality of the course and its materials – the sheer breadth of the topical coverage. We provide a thorough treatment of biology’s foundational concepts while condensing selected topics in response to the market’s request for a textbook with a scope that is manageable for instructors and students alike. We also strive to make biology, as a discipline, interesting and accessible to students. In addition to a comprehensive coverage of core concepts and foundational research, we have incorporated features that draw learners into the discipline in meaningful ways.

The pedagogical choices, chapter arrangements, and learning objective fulfillment were developed and vetted with the feedback of another one hundred reviewers, who thoroughly read the material and offered detailed critical commentary.

Pedagogical Foundation and Features

Biology is grounded on a solid scientific base and designed to help students understand the concepts at hand. Throughout the text, one can explore features that engage the students in scientific inquiry by taking selected topics a step further. Our features include:

- **Evolution Connection** features uphold the importance of evolution to all biological study through discussions like “The Evolution of Metabolic Pathways” and “Algae and Evolutionary Paths to Photosynthesis.”

- **Scientific Method Connection** call-outs walk students through actual or thought experiments that elucidate the steps of the scientific process as applied to the topic. Features include “Determining the Time Spent in Cell Cycle Stages” and “Testing the Hypothesis of Independent Assortment.”
- **Career Connection** features present information on a variety of careers in the biological sciences, introducing students to the educational requirements and day-to-day work life of a variety of professions, such as microbiologist, ecologist, neurologist, and forensic scientist.
- **Everyday Connection** features tie biological concepts to emerging issues and discuss science in terms of everyday life. Topics include “Chesapeake Bay” and “Can Snail Venom Be Used as a Pharmacological Pain Killer?”

Art and Animations That Engage

Our art program takes a straightforward approach designed to help students learn the concepts of biology through simple, effective illustrations, photos, and micrographs. *Biology* also incorporates links to relevant animations and interactive exercises that help bring biology to life for students.

- **Art Connection** features call out core figures in each chapter for student study. Questions about key figures, including clicker questions that can be used in the classroom, engage students’ critical thinking and analytical abilities to ensure their genuine understanding.
- **Link to Learning** features direct students to online interactive exercises and animations to add a fuller context and examples to core content.

About Our Team

Biology would not be possible if not for the tremendous contributions of the authors and community reviewing team.

Senior Contributors

Yael Avissar	Rhode Island College	Cell Biology
Jung Choi	Georgia Institute of Technology	Genetics
Jean DeSaix	University of North Carolina at Chapel Hill	Evolution
Vladimir Jurukovski	Suffolk County Community College	Animal Physiology
Robert Wise	University of Wisconsin, Oshkosh	Plant Biology
Connie Rye	east Mississippi Community College	General Content Lead

Faculty Contributors and Reviewers

Julie Adams	Aurora University
Summer Allen	Brown University

James Bader	Case Western Reserve University
David Bailey	St. Norbert College
Mark Belk	Brigham Young University
Nancy Boury	Iowa State University
Lisa Bonneau	Metropolitan Community College - Blue River
Graciela Brelles-Marino	California State University Pomona
Mark Browning	Purdue University
Sue Chaplin	University of St. Thomas
George Cline	Jacksonville State University
Deb Cook	Georgia Gwinnett College
Diane Day	Clayton State University
Frank Dirrigl	The University of Texas - Pan American
Waneene Dorsey	Grambling State University
Nick Downey	University of Wisconsin La Crosse
Rick Duhrkopf	Baylor University
Kristy Duran	Adams State University
Stan Eisen	Christian Brothers University
Brent Ewers	University of Wyoming

Myriam Feldman	Lake Washington Institute of Technology
Michael Fine	Virginia Commonwealth University
Linda Flora	Delaware County Community College
Thomas Freeland	Walsh University
David Gris�	Texas A & M University - Corpus Christi
Andrea Hazard	SUNY Cortland
Michael Hedrick	University of North Texas
Linda Hensel	Mercer University
Mark Kopeny	University of Virginia
Norman Johnson	University of Massachusetts - Amherst
Grace Lasker	Lake Washington Institute of Technology; Walden University
Sandy Latourelle	SUNY Plattsburgh
Theo Light	Shippensburg University
Clark Lindgren	Grinnell College
James Malcolm	University of Redlands
Mark Meade	Jacksonville State University
Richard Merritt	Houston Community College
James Mickle	North Carolina State University

Jasleen Mishra	Houston Community College
Dudley Moon	Albany College of Pharmacy and Health Sciences
Shobhana Natarajan	Brookhaven College
Jonas Okeagu	Fayetteville State University
Diana Oliveras	University of Colorado Boulder
John Peters	College of Charleston
Joel Piperberg	Millersville University
Johanna Porter-Kelley	Winston-Salem State university
Robyn Puffenbarger	Bridgewater College
Dennis Revie	California Lutheran University
Ann Rushing	Baylor University
Sangha Saha	City College of Chicago
Edward Saiff	Ramapo College of New Jersey
Brian Shmaefsky	Lone Star College System
Robert Sizemore	Alcorn State University
Marc Smith	Sinclair Community College
Frederick Spiegel	University of Arkansas

Frederick Sproull	La Roche College
Bob Sullivan	Marist College
Mark Sutherland	Hendrix College
Toure Thompson	Alabama A&M University
Scott Thomson	University of Wisconsin - Parkside
Allison van de Meene	University of Melbourne
Mary White	Southeastern Louisiana University
Steven Wilt	Bellarmino University
James Wise	Hampton University
Renna Wolfe	
Virginia Young	Mercer University
Leslie Zeman	University of Washington
Daniel Zurek	Pittsburg State University
Shobhana Natarajan	Alcon Laboratories, Inc.

Learning Resources

- Wiley Plus for Biology-Fall 2013 Pilot**
[WileyPLUS](#) provides an engaging online environment for effective teaching and learning. WileyPLUS builds students' confidence because it takes the guesswork out of studying by providing a clear

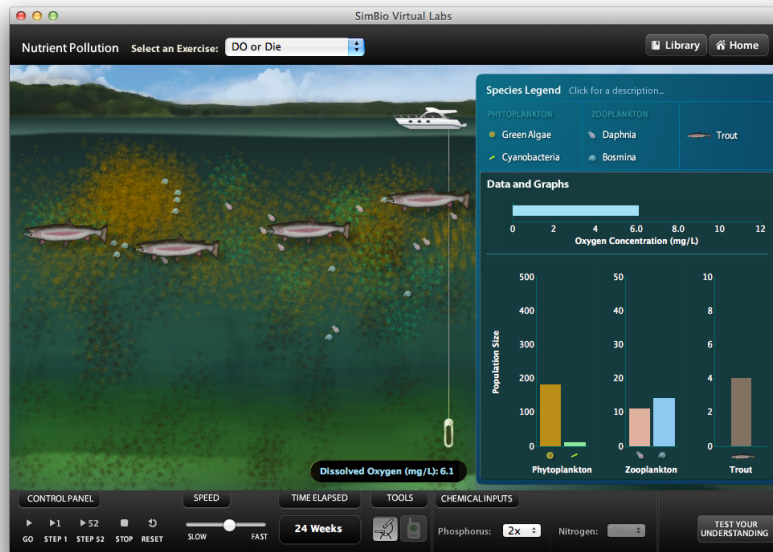
roadmap; what to do, how to do it, and if they did it right. With WileyPLUS, students take more initiative. Therefore, the course has a greater impact on their learning experience. Adaptive tools provide students with a personal, adaptive learning experience so they can build their proficiency on topics and use their study time most effectively. Please let us know if you would like to participate in a Fall 2013 Pilot.

- **Biology Powerpoint Slides (faculty only)**

The [PowerPoint slides](#) are based on the extensive illustrations from Biology. They can be edited, incorporated into lecture notes, and you are free to share with anyone in the community. This is a restricted item requiring faculty registration. NOTE: This file is very large and may take some time to download.

- **SimBio (Laboratory)**

[SimBio's interactive modules](#) (virtual labs and interactive tutorials and chapters) provide engaging, discovery-based learning tools that complement many of the chapters of Biology. SimBio is best known for their EcoBeaker® and EvoBeaker® suites of simulated ecology and evolution laboratories that guide students through the “discovery” of important concepts via a mix of structured and open-ended experimentation on simulated systems. In response to popular demand, SimBio has begun applying the same powerful approaches to topics in cell biology, genetics, and neurobiology. All of SimBio's modules include instant-feedback questions that enhance student comprehension and auto-graded questions that facilitate implementation.



Bis2A 01.0 Introduction to Bis2A v1.2
class="introduction"

This NASA image is a composite of several satellite-based views of Earth. To make the whole-Earth image, NASA scientists combine observations of different parts of the planet. (credit: NASA/GSFC/NOAA/USGS)

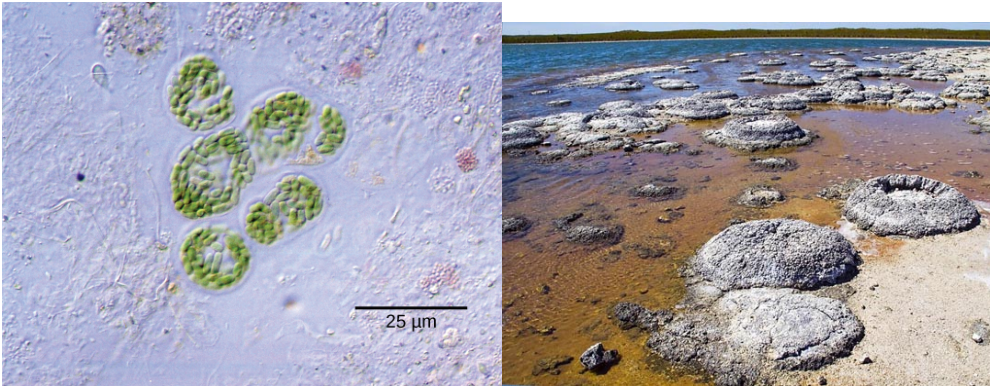


Viewed from space, Earth offers no clues about the diversity of life forms that reside there. The first forms of life on Earth are thought to have been microorganisms that existed for billions of years in the ocean before plants and animals appeared. The mammals, birds, and flowers so familiar to us are all relatively recent, originating 130 to 200 million years ago. Humans have inhabited this planet for only the last 2.5 million years, and only in the last 200,000 years have humans started looking like we do today.

Bis2A 01.1 The Science of Biology v1.2

By the end of this section, you will be able to:

- Identify the shared characteristics of the natural sciences
- Summarize the steps of the scientific method
- Compare inductive reasoning with deductive reasoning
- Describe the goals of basic science and applied science



Formerly called blue-green algae, these (a) cyanobacteria, shown here at 300x magnification under a light microscope, are some of Earth's oldest life forms.

These (b) stromatolites along the shores of Lake Thetis in Western Australia are ancient structures formed by the layering of cyanobacteria in shallow waters. (credit a: modification of work by NASA; credit b: modification of work by Ruth Ellison; scale-bar data from Matt Russell)

What is biology? In simple terms, **biology** is the study of living organisms and their interactions with one another and their environments. This is a very broad definition because the scope of biology is vast. Biologists may study anything from the microscopic or submicroscopic view of a cell to ecosystems and the whole living planet ([\[link\]](#)). Listening to the daily news, you will quickly realize how many aspects of biology are discussed every day. For example, recent news topics include *Escherichia coli* ([\[link\]](#)) outbreaks in spinach and *Salmonella* contamination in peanut butter. Other subjects include efforts toward finding a cure for AIDS, Alzheimer's

disease, and cancer. On a global scale, many researchers are committed to finding ways to protect the planet, solve environmental issues, and reduce the effects of climate change. All of these diverse endeavors are related to different facets of the discipline of biology.



Escherichia coli (*E. coli*) bacteria, seen in this scanning electron micrograph, are normal residents of our digestive tracts that aid in the absorption of vitamin K and other nutrients. However, virulent strains are sometimes responsible for disease outbreaks. (credit: Eric Erbe, digital colorization by Christopher Pooley, both of USDA, ARS, EMU)

The Process of Science

Biology is a science, but what exactly is science? What does the study of biology share with other scientific disciplines? **Science** (from the Latin *scientia*, meaning “knowledge”) can be defined as knowledge that covers general truths or the operation of general laws, especially when acquired and tested by the scientific method. It becomes clear from this definition

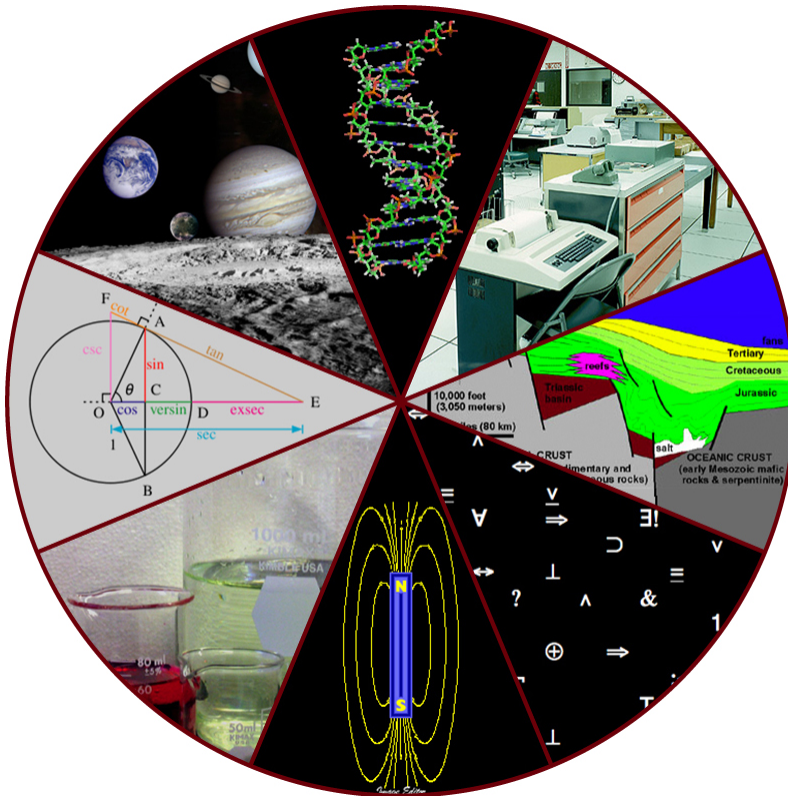
that the application of the scientific method plays a major role in science. The **scientific method** is a method of research with defined steps that include experiments and careful observation.

The steps of the scientific method will be examined in detail later, but one of the most important aspects of this method is the testing of hypotheses by means of repeatable experiments. A **hypothesis** is a suggested explanation for an event, which can be tested. Although using the scientific method is inherent to science, it is inadequate in determining what science is. This is because it is relatively easy to apply the scientific method to disciplines such as physics and chemistry, but when it comes to disciplines like archaeology, psychology, and geology, the scientific method becomes less applicable as it becomes more difficult to repeat experiments.

These areas of study are still sciences, however. Consider archeology—even though one cannot perform repeatable experiments, hypotheses may still be supported. For instance, an archeologist can hypothesize that an ancient culture existed based on finding a piece of pottery. Further hypotheses could be made about various characteristics of this culture, and these hypotheses may be found to be correct or false through continued support or contradictions from other findings. A hypothesis may become a verified theory. A **theory** is a tested and confirmed explanation for observations or phenomena. Science may be better defined as fields of study that attempt to comprehend the nature of the universe.

Natural Sciences

What would you expect to see in a museum of natural sciences? Frogs? Plants? Dinosaur skeletons? Exhibits about how the brain functions? A planetarium? Gems and minerals? Or, maybe all of the above? Science includes such diverse fields as astronomy, biology, computer sciences, geology, logic, physics, chemistry, and mathematics ([\[link\]](#)). However, those fields of science related to the physical world and its phenomena and processes are considered **natural sciences**. Thus, a museum of natural sciences might contain any of the items listed above.



The diversity of scientific fields includes astronomy, biology, computer science, geology, logic, physics, chemistry, mathematics, and many other fields. (credit: “Image Editor”/Flickr)

There is no complete agreement when it comes to defining what the natural sciences include, however. For some experts, the natural sciences are astronomy, biology, chemistry, earth science, and physics. Other scholars choose to divide natural sciences into **life sciences**, which study living things and include biology, and **physical sciences**, which study nonliving matter and include astronomy, geology, physics, and chemistry. Some disciplines such as biophysics and biochemistry build on both life and physical sciences and are interdisciplinary. Natural sciences are sometimes referred to as “hard science” because they rely on the use of quantitative data; social sciences that study society and human behavior are more likely to use qualitative assessments to drive investigations and findings.

Not surprisingly, the natural science of biology has many branches or subdisciplines. Cell biologists study cell structure and function, while biologists who study anatomy investigate the structure of an entire organism. Those biologists studying physiology, however, focus on the internal functioning of an organism. Some areas of biology focus on only particular types of living things. For example, botanists explore plants, while zoologists specialize in animals.

Scientific Reasoning

One thing is common to all forms of science: an ultimate goal “to know.” Curiosity and inquiry are the driving forces for the development of science. Scientists seek to understand the world and the way it operates. To do this, they use two methods of logical thinking: inductive reasoning and deductive reasoning.

Inductive reasoning, “from the bottom up”, is a form of logical thinking that uses related observations to arrive at a general conclusion. This type of reasoning is common in descriptive science. A life scientist such as a biologist makes observations and records them. These data can be qualitative or quantitative, and the raw data can be supplemented with drawings, pictures, photos, or videos. From many observations, the scientist can infer conclusions (inductions) based on evidence. Inductive reasoning involves formulating generalizations inferred from careful observation and the analysis of a large amount of data. Brain studies provide an example. In this type of research, many live brains are observed while people are doing a specific activity, such as viewing images of food. The part of the brain that “lights up” during this activity is then predicted to be the part controlling the response to the selected stimulus, in this case, images of food. The “lighting up” of the various areas of the brain is caused by excess absorption of radioactive sugar derivatives by active areas of the brain. The resultant increase in radioactivity is observed by a scanner. Then, researchers can stimulate that part of the brain to see if similar responses result.

An example of inductive reasoning

- This bee stung me. It is a hymenopteran.
- This wasp has stung me. It is a hymenopteran.
- This fire ant stung me. It is a hymenopteran.
- I'm starting to see a pattern here. All hymenopterans have stingers.

Deductive reasoning or deduction is the type of logic used in hypothesis-based science. In deductive reason, the pattern of thinking moves in the opposite direction as compared to inductive reasoning. **Deductive reasoning**, "from the top down", is a form of logical thinking that uses a general principle or law to forecast specific results. From those general principles, a scientist can extrapolate and predict the specific results that would be valid as long as the general principles are valid. Studies in climate change can illustrate this type of reasoning. For example, scientists may predict that if the climate becomes warmer in a particular region, then the distribution of plants and animals should change. These predictions have been made and tested, and many such changes have been found, such as the modification of arable areas for agriculture, with change based on temperature averages.

An example of deductive reasoning

- All wasps have stingers.
- This thing in my hand is a wasp.
- Therefore, this thing can probably sting me!

Both types of logical thinking are related to the two main pathways of scientific study: descriptive science and hypothesis-based science.

Descriptive (or discovery) science, which is usually inductive, aims to observe, explore, and discover, while **hypothesis-based science**, which is usually deductive, begins with a specific question or problem and a potential answer or solution that can be tested. The boundary between these two forms of study is often blurred, and most scientific endeavors combine both approaches. The fuzzy boundary becomes apparent when thinking about how easily observation can lead to specific questions. For example, a gentleman in the 1940s observed that the burr seeds that stuck to his clothes and his dog's fur had a tiny hook structure. On closer inspection, he discovered that the burrs' gripping device was more reliable than a zipper. He eventually developed a company and produced the hook-and-loop

fastener popularly known today as Velcro. Descriptive science and hypothesis-based science are in continuous dialogue.

The above examples are from

- [Inductive and Deductive reasoning](#)

For a more modern perspective try this link from the Big Bang Theory

- [Big Bang Theory on the Scientific Method](#).

The Scientific Method

Biologists study the living world by posing questions about it and seeking science-based responses. This approach is common to other sciences as well and is often referred to as the scientific method. The scientific method was used even in ancient times, but it was first documented by England's Sir Francis Bacon (1561–1626) ([\[link\]](#)), who set up inductive methods for scientific inquiry. The scientific method is not exclusively used by biologists but can be applied to almost all fields of study as a logical, rational problem-solving method.



Sir Francis Bacon
(1561–1626) is
credited with being
the first to define
the scientific
method. (credit:
Paul van Somer)

The scientific process typically starts with an observation (often a problem to be solved) that leads to a question. Let's think about a simple problem that starts with an observation and apply the scientific method to solve the problem. One Monday morning, a student arrives at class and quickly discovers that the classroom is too warm. That is an observation that also describes a problem: the classroom is too warm. The student then asks a question: "Why is the classroom so warm?"

Proposing a Hypothesis

Recall that a hypothesis is a suggested explanation that can be tested. To solve a problem, several hypotheses may be proposed. For example, one hypothesis might be, "The classroom is warm because no one turned on the air conditioning." But there could be other responses to the question, and therefore other hypotheses may be proposed. A second hypothesis might be, "The classroom is warm because there is a power failure, and so the air conditioning doesn't work."

Once a hypothesis has been selected, the student can make a prediction. A prediction is similar to a hypothesis but it typically has the format "If . . . then" For example, the prediction for the first hypothesis might be, "*If* the student turns on the air conditioning, *then* the classroom will no longer be too warm."

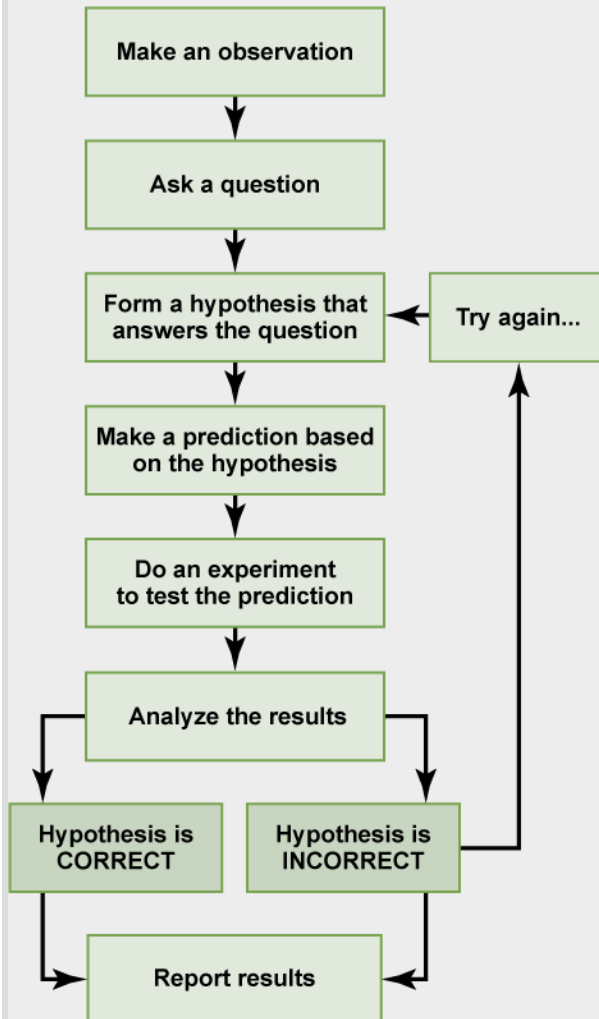
Testing a Hypothesis

A valid hypothesis must be testable. It should also be **falsifiable**, meaning that it can be disproven by experimental results. Importantly, science does not claim to “prove” anything because scientific understandings are always subject to modification with further information. This step—openness to disproving ideas—is what distinguishes sciences from non-sciences. The presence of the supernatural, for instance, is neither testable nor falsifiable. To test a hypothesis, a researcher will conduct one or more experiments designed to eliminate one or more of the hypotheses. Each experiment will have one or more variables and one or more controls. A **variable** is any part of the experiment that can vary or change during the experiment. The **control group** contains every feature of the experimental group except it is not given the manipulation that is hypothesized about. Therefore, if the results of the experimental group differ from the control group, the difference must be due to the hypothesized manipulation, rather than some outside factor. Look for the variables and controls in the examples that follow. To test the first hypothesis, the student would find out if the air conditioning is on. If the air conditioning is turned on but does not work, there should be another reason, and this hypothesis should be rejected. To test the second hypothesis, the student could check if the lights in the classroom are functional. If so, there is no power failure and this hypothesis should be rejected. Each hypothesis should be tested by carrying out appropriate experiments. Be aware that rejecting one hypothesis does not determine whether or not the other hypotheses can be accepted; it simply eliminates one hypothesis that is not valid ([\[link\]](#)). Using the scientific method, the hypotheses that are inconsistent with experimental data are rejected.

While this “warm classroom” example is based on observational results, other hypotheses and experiments might have clearer controls. For instance, a student might attend class on Monday and realize she had difficulty concentrating on the lecture. One observation to explain this occurrence might be, “When I eat breakfast before class, I am better able to pay attention.” The student could then design an experiment with a control to test this hypothesis.

Note:

Art Connection



The scientific method consists of a series of well-defined steps. If a hypothesis is not supported by experimental data, a new hypothesis can be proposed.

In the example below, the scientific method is used to solve an everyday problem. Order the scientific method steps (numbered items) with the process of solving the everyday problem (lettered items). Then, based on the results of the experiment, is the hypothesis correct? If it is incorrect, propose some alternative hypotheses.

1. Observation
2. Question
3. Hypothesis (answer)
4. Prediction
5. Experiment
6. Result

- a. There is something wrong with the electrical outlet.
- b. If something is wrong with the outlet, my coffeemaker also won't work when plugged into it.
- c. My toaster doesn't toast my bread.
- d. I plug my coffee maker into the outlet.
- e. My coffeemaker works.
- f. Why doesn't my toaster work?

In hypothesis-based science, specific results are predicted from a general premise. This type of reasoning is called deductive reasoning: deduction proceeds from the general to the particular. But the reverse of the process is also possible: sometimes, scientists reach a general conclusion from a number of specific observations. This type of reasoning is called inductive reasoning, and it proceeds from the particular to the general. Inductive and deductive reasoning are often used in tandem to advance scientific knowledge ([link](#)).

Note:

Art Connection

Two Types of Reasoning	
Inductive reasoning: from a number of observations, a general conclusion is drawn.	Deductive reasoning: from a general premise, specific results are predicted.
Observations <ul style="list-style-type: none"> • Members of a species are not all the same. • Individuals compete for resources. • Species are generally adapted to their environment. 	General premise Individuals most adapted to their environment are more likely to survive and pass their traits on to the next generation.
↓	↓
Conclusion Individuals most adapted to their environment are more likely to survive and pass their traits to the next generation.	Predicted results If the average temperature in an ecosystem increases due to climate change, individuals better adapted to warmer temperatures will outcompete those that are not.

Scientists use two types of reasoning, inductive and deductive reasoning, to advance scientific knowledge. As is the case in this example, the conclusion from inductive reasoning can often become the premise for inductive reasoning.

Decide if each of the following is an example of inductive or deductive reasoning.

1. All flying birds and insects have wings. Birds and insects flap their wings as they move through the air. Therefore, wings enable flight.
2. Insects generally survive mild winters better than harsh ones. Therefore, insect pests will become more problematic if global temperatures increase.

3. Chromosomes, the carriers of DNA, separate into daughter cells during cell division. Therefore, DNA is the genetic material.
4. Animals as diverse as humans, insects, and wolves all exhibit social behavior. Therefore, social behavior must have an evolutionary advantage.

The scientific method may seem too rigid and structured. It is important to keep in mind that, although scientists often follow this sequence, there is flexibility. Sometimes an experiment leads to conclusions that favor a change in approach; often, an experiment brings entirely new scientific questions to the puzzle. Many times, science does not operate in a linear fashion; instead, scientists continually draw inferences and make generalizations, finding patterns as their research proceeds. Scientific reasoning is more complex than the scientific method alone suggests. Notice, too, that the scientific method can be applied to solving problems that aren't necessarily scientific in nature.

How Bis2A will be taught

BIS 2A the first course in the Biological Sciences lower division core sequence. This sequence provides a foundation in modern biology for a broad range of majors. In BIS2A we introduce you to the fundamental chemical, molecular, genetic, and cellular building blocks of living organisms and universal core concepts in biology. There is a heavy focus on the fundamental unit of living systems, the cell. In BIS 2B you will examine ecological and evolutionary processes that shape biological diversity. Finally in BIS 2C you will examine biological diversity in detail. BIS2A is intended to provide you with foundational knowledge that you will build on in 2B and 2C and carry with you throughout your subsequent courses. We will stress important concepts but will also expect you to learn some of the vocabulary of Biology. This should be fun!

BIS 2A focuses on developing your understanding of several core concepts in biology that can be applied in contexts beyond the boundaries of this

course. We expect that once you have successfully completed this course that you will be able to:

- 1. Apply principles of chemistry and bioenergetics in the context of biological systems to describe how cells acquire and transform energy to fuel various life sustaining processes, including chemical transformations of elemental compounds, cellular replication, and cellular information processing.
- 2. Explain the relationship between genotype and key genetic processes that create phenotypic diversity.
- 3. Describe the processes regulating the management of cellular information; how information is stored, read, rearranged, replicated; how cells interact with their environment and how these processes can control cellular physiology. Insert paragraph text here.

Art Connections

Exercise:

Problem:

[\[link\]](#) Decide if each of the following is an example of inductive or deductive reasoning.

1. All flying birds and insects have wings. Birds and insects flap their wings as they move through the air. Therefore, wings enable flight.
2. Insects generally survive mild winters better than harsh ones. Therefore, insect pests will become more problematic if global temperatures increase.
3. Chromosomes, the carriers of DNA, separate into daughter cells during cell division. Therefore, DNA is the genetic material.
4. Animals as diverse as humans, insects, and wolves all exhibit social behavior. Therefore, social behavior must have an evolutionary advantage.

Solution:

[\[link\]](#) 1: inductive; 2: deductive; 3: deductive; 4: inductive.

Review Questions

Exercise:

Problem: The first forms of life on Earth were _____.

- a. plants
- b. microorganisms
- c. birds
- d. dinosaurs

Solution:

B

Exercise:

Problem:

A suggested and testable explanation for an event is called a _____.

- a. hypothesis
- b. variable
- c. theory
- d. control

Solution:

A

Exercise:

Problem:

The type of logical thinking that uses related observations to arrive at a general conclusion is called _____.

- a. deductive reasoning
- b. the scientific method
- c. hypothesis-based science
- d. inductive reasoning

Solution:

D

Exercise:**Problem:**

A person notices that her houseplants that are regularly exposed to music seem to grow more quickly than those in rooms with no music. As a result, she determines that plants grow better when exposed to music. This example most closely resembles which type of reasoning?

- a. inductive reasoning
- b. deductive reasoning
- c. neither, because no hypothesis was made
- d. both inductive and deductive reasoning

Solution:

A

Free Response**Exercise:**

Problem:

Although the scientific method is used by most of the sciences, it can also be applied to everyday situations. Think about a problem that you may have at home, at school, or with your car, and apply the scientific method to solve it.

Solution:

Answers will vary, but should apply the steps of the scientific method. One possibility could be a car which doesn't start. The hypothesis could be that the car doesn't start because the battery is dead. The experiment would be to change the battery or to charge the battery and then check whether the car starts or not. If it starts, the problem was due to the battery, and the hypothesis is accepted.

Exercise:**Problem:**

Give an example of how applied science has had a direct effect on your daily life.

Solution:

Answers will vary. One example of how applied science has had a direct effect on daily life is the presence of vaccines. Vaccines to prevent diseases such as polio, measles, tetanus, and even influenza affect daily life by contributing to individual and societal health.

Glossary**biology**

the study of living organisms and their interactions with one another and their environments

deductive reasoning

form of logical thinking that uses a general inclusive statement to forecast specific results

falsifiable

able to be disproven by experimental results

hypothesis

suggested explanation for an observation, which can be tested

hypothesis-based science

form of science that begins with a specific question and potential testable answers

inductive reasoning

form of logical thinking that uses related observations to arrive at a general conclusion

life science

field of science, such as biology, that studies living things

natural science

field of science that is related to the physical world and its phenomena and processes

physical science

field of science, such as geology, astronomy, physics, and chemistry, that studies nonliving matter

science

knowledge that covers general truths or the operation of general laws, especially when acquired and tested by the scientific method

scientific method

method of research with defined steps that include observation, formulation of a hypothesis, testing, and confirming or falsifying the hypothesis

serendipity

fortunate accident or a lucky surprise

theory

tested and confirmed explanation for observations or phenomena

variable

part of an experiment that the experimenter can vary or change

Bis2A 01.2 Themes and Concepts of Biology

By the end of this section, you will be able to:

- Identify and describe the properties of life
- Describe the levels of organization among living things
- Recognize and interpret a phylogenetic tree

Biology is the science that studies life, but what exactly is life? This may sound like a silly question with an obvious response, but it is not always easy to define life. For example, a branch of biology called virology studies viruses, which exhibit some of the characteristics of living entities but lack others. It turns out that although viruses can attack living organisms, cause diseases, and even reproduce, they do not meet the criteria that biologists use to define life. Consequently, virologists are not biologists, strictly speaking. Similarly, some biologists study the early molecular evolution that gave rise to life; since the events that preceded life are not biological events, these scientists are also excluded from biology in the strict sense of the term.

From its earliest beginnings, biology has wrestled with three questions: What are the shared properties that make something “alive”? And once we know something is alive, how do we find meaningful levels of organization in its structure? And, finally, when faced with the remarkable diversity of life, how do we organize the different kinds of organisms so that we can better understand them? As new organisms are discovered every day, biologists continue to seek answers to these and other questions.

Properties of Life

All living organisms share several key characteristics or functions: order, sensitivity or response to the environment, reproduction, adaptation, growth and development, regulation, homeostasis, energy processing, and evolution. When viewed together, these nine characteristics serve to define life.

Order



A toad represents a highly organized structure consisting of cells, tissues, organs, and organ systems. (credit: “Ivengo”/Wikimedia Commons)

Organisms are highly organized, coordinated structures that consist of one or more cells. Even very simple, single-celled organisms are remarkably complex: inside each cell, atoms make up molecules; these in turn make up cell organelles and other cellular inclusions. In multicellular organisms ([link](#)), similar cells form tissues. Tissues, in turn, collaborate to create organs (body structures with a distinct function). Organs work together to form organ systems.

Sensitivity or Response to Stimuli



The leaves of this sensitive plant (*Mimosa pudica*) will instantly droop and fold when touched. After a few minutes, the plant returns to normal. (credit: Alex Lomas)

Organisms respond to diverse stimuli. For example, plants can bend toward a source of light, climb on fences and walls, or respond to touch ([\[link\]](#)). Even tiny bacteria can move toward or away from chemicals (a process called *chemotaxis*) or light (*phototaxis*). Movement toward a stimulus is considered a positive response, while movement away from a stimulus is considered a negative response.

Examples of sensitivity to stimuli

- [Time-lapse of plant response to light.](#)

Note:

Link to Learning



Watch [this video](#) to see how plants respond to a stimulus—from opening to light, to wrapping a tendril around a branch, to capturing prey.

Reproduction

Single-celled organisms reproduce by first duplicating their DNA, and then dividing it equally as the cell prepares to divide to form two new cells. Multicellular organisms often produce specialized reproductive germline cells that will form new individuals. When reproduction occurs, genes containing DNA are passed along to an organism's offspring. These genes ensure that the offspring will belong to the same species and will have similar characteristics, such as size and shape.

Growth and Development

Organisms grow and develop following specific instructions coded for by their genes. These genes provide instructions that will direct cellular growth and development, ensuring that a species' young ([link](#)) will grow up to exhibit many of the same characteristics as its parents.



Although no two look alike, these kittens have inherited genes from both parents and share many of the same characteristics. (credit: Rocky Mountain Feline Rescue)

Regulation

Even the smallest organisms are complex and require multiple regulatory mechanisms to coordinate internal functions, respond to stimuli, and cope with environmental stresses. Two examples of internal functions regulated in an organism are nutrient transport and blood flow. Organs (groups of tissues working together) perform specific functions, such as carrying oxygen throughout the body, removing wastes, delivering nutrients to every cell, and cooling the body.

Homeostasis



Polar bears (*Ursus maritimus*) and other mammals living in ice-covered regions maintain their body temperature by generating heat and reducing heat loss through thick fur and a dense layer of fat under their skin. (credit: “longhorndave”/Flickr)

In order to function properly, cells need to have appropriate conditions such as proper temperature, pH, and appropriate concentration of diverse chemicals. These conditions may, however, change from one moment to the next. Organisms are able to maintain internal conditions within a narrow range almost constantly, despite environmental changes, through **homeostasis** (literally, “steady state”)—the ability of an organism to maintain constant internal conditions. For example, an organism needs to regulate body temperature through a process known as thermoregulation. Organisms that live in cold climates, such as the polar bear ([\[link\]](#)), have body structures that help them withstand low temperatures and conserve body heat. Structures that aid in this type of insulation include fur, feathers, blubber, and fat. In hot climates, organisms have methods (such as perspiration in humans or panting in dogs) that help them to shed excess body heat. For more information on homeostasis visit the Khan Academy link [homeostasis](#).

Energy Processing



The California condor (*Gymnogyps californianus*) uses chemical energy derived from food to power flight. California condors are an endangered species; this bird has a wing tag that helps biologists identify the individual. (credit: Pacific Southwest Region U.S. Fish and Wildlife Service)

All organisms use a source of energy for their metabolic activities. Some organisms capture energy from the sun and convert it into chemical energy

in food; others use chemical energy in molecules they take in as food ([link](#)).

Which of the above characteristics of life can apply to the items below?

- a. Fire
- b. Salt Crystals
- c. Computer
- d. Truck

- For each choice below, can you explain how?
- Fire
- Salt Crystals
- Computer
- Truck

Levels of Organization of Living Things

Living things are highly organized and structured, following a hierarchy that can be examined on a scale from small to large. The **atom** is the smallest and most fundamental unit of matter. It consists of a nucleus surrounded by electrons. Atoms form molecules. A **molecule** is a chemical structure consisting of at least two atoms held together by one or more chemical bonds. Many molecules that are biologically important are **macromolecules**, large molecules that are typically formed by polymerization (a polymer is a large molecule that is made by combining smaller units called monomers, which are simpler than macromolecules). An example of a macromolecule is deoxyribonucleic acid (DNA) ([link](#)), which contains the instructions for the structure and functioning of all living organisms.



All molecules, including this DNA molecule, are composed of atoms. (credit: “brian0918”/Wikimedia Commons. For a 3D animation click [here](#)).

Note:
Link to Learning



Watch [this video](#) that animates the three-dimensional structure of the DNA molecule shown in [\[link\]](#).

Some cells contain aggregates of macromolecules surrounded by membranes; these are called **organelles**. Organelles are small structures that exist within cells. Examples of organelles include mitochondria and chloroplasts, which carry out indispensable functions: mitochondria produce energy to power the cell, while chloroplasts enable green plants to utilize the energy in sunlight to make sugars. All living things are made of cells; the **cell** itself is the smallest fundamental unit of structure and function in living organisms. (This requirement is why viruses are not considered living: they are not made of cells. To make new viruses, they have to invade and hijack the reproductive mechanism of a living cell; only then can they obtain the materials they need to reproduce.) Some organisms consist of a single cell and others are multicellular. Cells are sometimes classified as prokaryotic (consisting of **Bacteria** and **Archaea**) or eukaryotic (**Eukarya**). Bacteria, Archaea and Eukarya, comprise the three kingdoms of life, each representing a distinct cellular lineage. **Prokaryotes** are single-celled or colonial organisms that do not have membrane-bound nuclei; in contrast, the cells of **eukaryotes** do have membrane-bound organelles and a membrane-bound nucleus. It should be noted that while the term prokaryote or prokaryotic is frequently used to discuss the similarities between bacteria and archaea and their common differences with eukaryotes, bacteria and archaea are as different from each other as they are different from eukaryotes. As we will discuss later, from an evolutionary perspective archaea are actually more closely related to eukaryotes than they are to bacteria. So why the common term prokaryote, it is an easy way to distinguish the simple structural similarities between bacteria and archaea

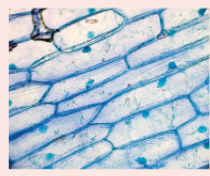
as opposed to the more complex cellular structure of eukaryotes. This can easily be visualized by looking at [\[link\]](#).

In larger organisms, cells combine to make **tissues**, which are groups of similar cells carrying out similar or related functions. **Organs** are collections of tissues grouped together performing a common function. Organs are present not only in animals but also in plants. An **organ system** is a higher level of organization that consists of functionally related organs. Mammals have many organ systems. For instance, the circulatory system transports blood through the body and to and from the lungs; it includes organs such as the heart and blood vessels. **Organisms** are individual living entities. For example, each tree in a forest is an organism. Single-celled prokaryotes and single-celled eukaryotes are also considered organisms and are typically referred to as microorganisms.

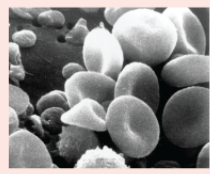
All the individuals of a species living within a specific area are collectively called a **population**. For example, a forest may include many pine trees. All of these pine trees represent the population of pine trees in this forest. Different populations may live in the same specific area. For example, the forest with the pine trees includes populations of flowering plants and also insects and microbial populations. A **community** is the sum of populations inhabiting a particular area. For instance, all of the trees, flowers, insects, and other populations in a forest form the forest's community. The forest itself is an ecosystem. An **ecosystem** consists of all the living things in a particular area together with the abiotic, non-living parts of that environment such as nitrogen in the soil or rain water. At the highest level of organization ([\[link\]](#)), the **biosphere** is the collection of all ecosystems, and it represents the zones of life on earth. It includes land, water, and even the atmosphere to a certain extent.

Note:

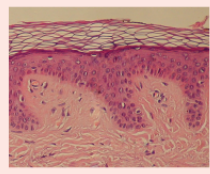
Art Connection



Organelles: The nucleus, dyed blue in these onion cells, is an example of an organelle.



Cells: Human blood cells.



Tissues: Human skin tissue.



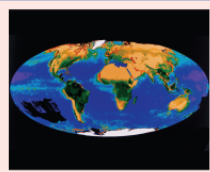
Organs and Organ Systems: Organs, such as the stomach and intestine, make up the human digestive system.



Organisms, Populations, and Communities: In a forest, each pine tree is an organism. Together, all the pine trees make up a population. All the plant and animal species in the forest comprise a community.



Ecosystems: This coastal ecosystem in the southeastern United States includes living organisms and the environment in which they live.



The Biosphere: Encompasses all the ecosystems on Earth.

The biological levels of organization of living things are shown. From a single organelle to the

entire biosphere, living organisms are parts of a highly structured hierarchy. (credit “organelles”: modification of work by Umberto Salvagnin; credit “cells”: modification of work by Bruce Wetzel, Harry Schaefer/ National Cancer Institute; credit “tissues”: modification of work by Kilbad; Fama Clamosa; Mikael Häggström; credit “organs”: modification of work by Mariana Ruiz Villareal; credit “organisms”: modification of work by "Crystal"/Flickr; credit “ecosystems”: modification of work by US Fish and Wildlife Service Headquarters; credit “biosphere”: modification of work by NASA)

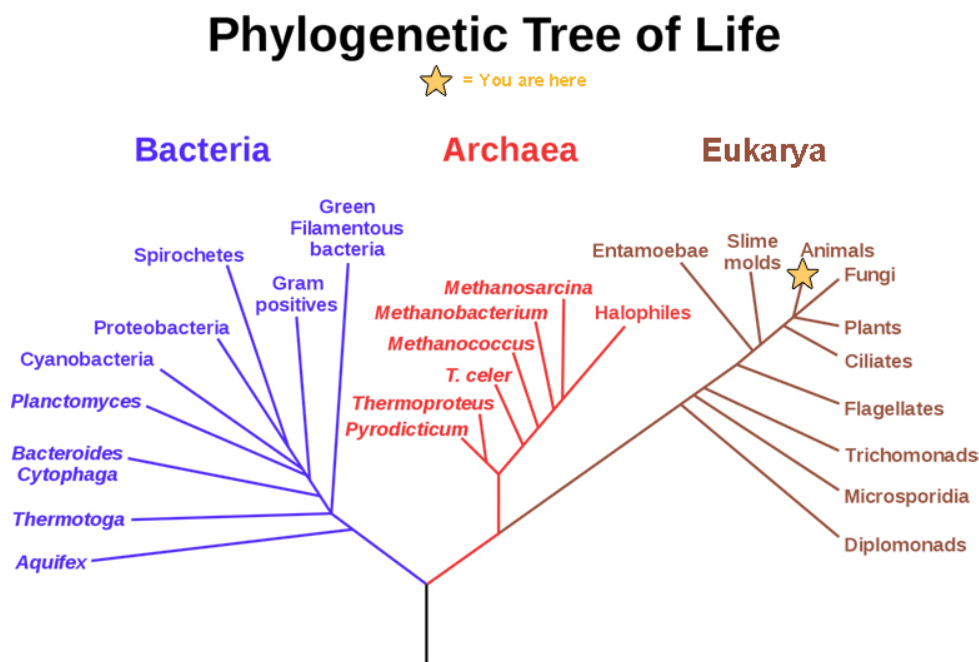
Which of the following statements is false?

- a. Tissues exist within organs which exist within organ systems.
- b. Communities exist within populations which exist within ecosystems.
- c. Organelles exist within cells which exist within tissues.
- d. Communities exist within ecosystems which exist in the biosphere.

The Diversity of Life

The fact that biology, as a science, has such a broad scope has to do with the tremendous diversity of life on earth. The source of this diversity is **evolution**, the process of gradual change during which new species arise from older species. Evolutionary biologists study the evolution of living things in everything from the microscopic world to ecosystems.

The evolution of various life forms on Earth can be summarized in a phylogenetic tree ([\[link\]](#)). A **phylogenetic tree** is a diagram showing the evolutionary relationships among biological species based on similarities and differences in genetic or physical traits or both. A phylogenetic tree is composed of nodes and branches. The internal nodes represent ancestors and are points in evolution when, based on scientific evidence, an ancestor is thought to have diverged to form two new species. The length of each branch is proportional to the time elapsed since the split.



This phylogenetic tree was constructed by microbiologist Carl Woese using data obtained from sequencing ribosomal RNA genes. The tree shows the separation of living organisms into three domains: Bacteria, Archaea, and Eukarya. Bacteria and Archaea are prokaryotes, single-celled organisms lacking intracellular organelles. (credit: Eric Gaba; NASA Astrobiology Institute)

Using figure 8, which of the following statements are true and which are false:

1. This tree shows that Halophiles is more related to Methanosarcina than it is to Proteobacteria.
2. This tree shows that Diplomanads and Halophiles and Thermotoga are all related by a common ancestor.
3. This tree shows that Eukaryotes are the most evolved.
4. This tree shows that each kingdom of life is highly diverse.

Note:

Evolution Connection

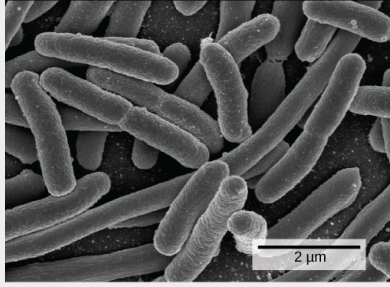
Carl Woese and the Phylogenetic Tree

In the past, biologists grouped living organisms into five kingdoms: animals, plants, fungi, protists, and bacteria. The organizational scheme was based mainly on physical features, as opposed to physiology, biochemistry, or molecular biology, all of which are used by modern systematics. The pioneering work of American microbiologist Carl Woese in the early 1970s has shown, however, that life on Earth has evolved along three lineages, now called domains—Bacteria, Archaea, and Eukarya. The first two are prokaryotic cells with microbes that lack membrane-enclosed nuclei and organelles. The third domain contains the eukaryotes and includes unicellular microorganisms together with the four original kingdoms (excluding bacteria). Woese defined Archaea as a new domain, and this resulted in a new taxonomic tree ([\[link\]](#)). Many organisms

belonging to the Archaea domain live under extreme conditions and are called extremophiles. To construct his tree, Woese used genetic relationships rather than similarities based on morphology (shape).

Woese's tree was constructed from comparative sequencing of the genes that are universally distributed, present in every organism, and conserved (meaning that these genes have remained essentially unchanged throughout evolution). Woese's approach was revolutionary because comparisons of physical features are insufficient to differentiate between the prokaryotes that appear fairly similar in spite of their tremendous biochemical diversity and genetic variability ([\[link\]](#)). The comparison of homologous DNA and RNA sequences provided Woese with a sensitive device that revealed the extensive variability of prokaryotes, and which justified the separation of the prokaryotes into two domains: bacteria and archaea.

These images represent different domains. The (a) bacteria in this micrograph belong to Domain Bacteria, while the (b) extremophiles (not visible) living in this hot vent belong to Domain Archaea. Both the (c) sunflower and (d) lion are part of Domain Eukarya. (credit a: modification of work by Drew March; credit b: modification of work by Steve Jurvetson; credit c: modification of work by Michael Arrighi; credit d: modification of work by Leszek Leszcynski)



(a)



(b)



(c)



(d)

Section Summary

Biology is the science of life. All living organisms share several key properties such as order, sensitivity or response to stimuli, reproduction, growth and development, regulation, homeostasis, and energy processing. Living things are highly organized parts of a hierarchy that includes atoms, molecules, organelles, cells, tissues, organs, and organ systems. Organisms, in turn, are grouped as populations, communities, ecosystems, and the biosphere. The great diversity of life today evolved from less-diverse ancestral organisms over billions of years. A diagram called a phylogenetic tree can be used to show evolutionary relationships among organisms.

Biology is very broad and includes many branches and subdisciplines. Examples include molecular biology, microbiology, neurobiology, zoology, and botany, among others.

Art Connections

Exercise:

Problem: [\[link\]](#) Which of the following statements is false?

- a. Tissues exist within organs which exist within organ systems.
- b. Communities exist within populations which exist within ecosystems.
- c. Organelles exist within cells which exist within tissues.
- d. Communities exist within ecosystems which exist in the biosphere.

Solution:

[\[link\]](#) Communities exist within populations which exist within ecosystems.

Review Questions

Exercise:

Problem:

The smallest unit of biological structure that meets the functional requirements of “living” is the _____.

- a. organ
- b. organelle
- c. cell
- d. macromolecule

Solution:

C

Free Response

Exercise:

Problem:

Select two items that biologists agree are necessary in order to consider an organism “alive.” For each, give an example of a non-living object that otherwise fits the definition of “alive,”

Solution:

Answers will vary. Layers of sedimentary rock have order but are not alive. Technology is capable of regulation but is not, of itself, alive.

Exercise:

Problem:

Consider the levels of organization of the biological world, and place each of these items in order from smallest level of organization to most encompassing: skin cell, elephant, water molecule, planet Earth, tropical rainforest, hydrogen atom, wolf pack, liver.

Solution:

Smallest level of organization to largest: hydrogen atom, water molecule, skin cell, liver, elephant, wolf pack, tropical rainforest, planet Earth

Exercise:

Problem:

You go for a long walk on a hot day. Give an example of a way in which homeostasis keeps your body healthy.

Solution:

During your walk, you may begin to perspire, which cools your body and helps your body to maintain a constant internal temperature. You

might also become thirsty and pause long enough for a cool drink, which will help to restore the water lost during perspiration.

Exercise:

Problem:

Using examples, explain how biology can be studied from a microscopic approach to a global approach.

Solution:

Researchers can approach biology from the smallest to the largest, and everything in between. For instance, an ecologist may study a population of individuals, the population's community, the community's ecosystem, and the ecosystem's part in the biosphere. When studying an individual organism, a biologist could examine the cell and its organelles, the tissues that the cells make up, the organs and their respective organ systems, and the sum total—the organism itself.

Glossary

Archaea

a member of one of the three kingdoms of life along with bacteria and eukarya, characterized by a lack of organelles and a unique lipid membrane

atom

smallest and most fundamental unit of matter

Bacteria

a member of one of the three kingdoms of life along with archaea and eukarya, characterized by a lack of organelles, unique cell wall material (peptidoglycan, and unique transcriptional, translational and replicative machinery

biosphere

collection of all the ecosystems on Earth

cell

smallest fundamental unit of structure and function in living things

community

set of populations inhabiting a particular area

ecosystem

all the living things in a particular area together with the abiotic, nonliving parts of that environment

eukaryote

organism with cells that have nuclei and membrane-bound organelles, and a member of one of the three kingdoms of life (Eukarya) along with archaea and bacteria

evolution

process of gradual change during which new species arise from older species and some species become extinct

homeostasis

ability of an organism to maintain constant internal conditions

macromolecule

large molecule, typically formed by the joining of smaller molecules

molecule

chemical structure consisting of at least two atoms held together by one or more chemical bonds

organ

collection of related tissues grouped together performing a common function

organ system

level of organization that consists of functionally related interacting organs

organelle

small structures that exist within cells and carry out cellular functions

organism

individual living entity

phylogenetic tree

diagram showing the evolutionary relationships among various biological species based on similarities and differences in genetic or physical traits or both; in essence, a hypothesis concerning evolutionary connections

population

all of the individuals of a species living within a specific area

prokaryote

single-celled organism that lacks organelles and does not have nuclei surrounded by a nuclear membrane

tissue

group of similar cells carrying out related functions

Bis2A 02.0 Introduction Chemistry of Life

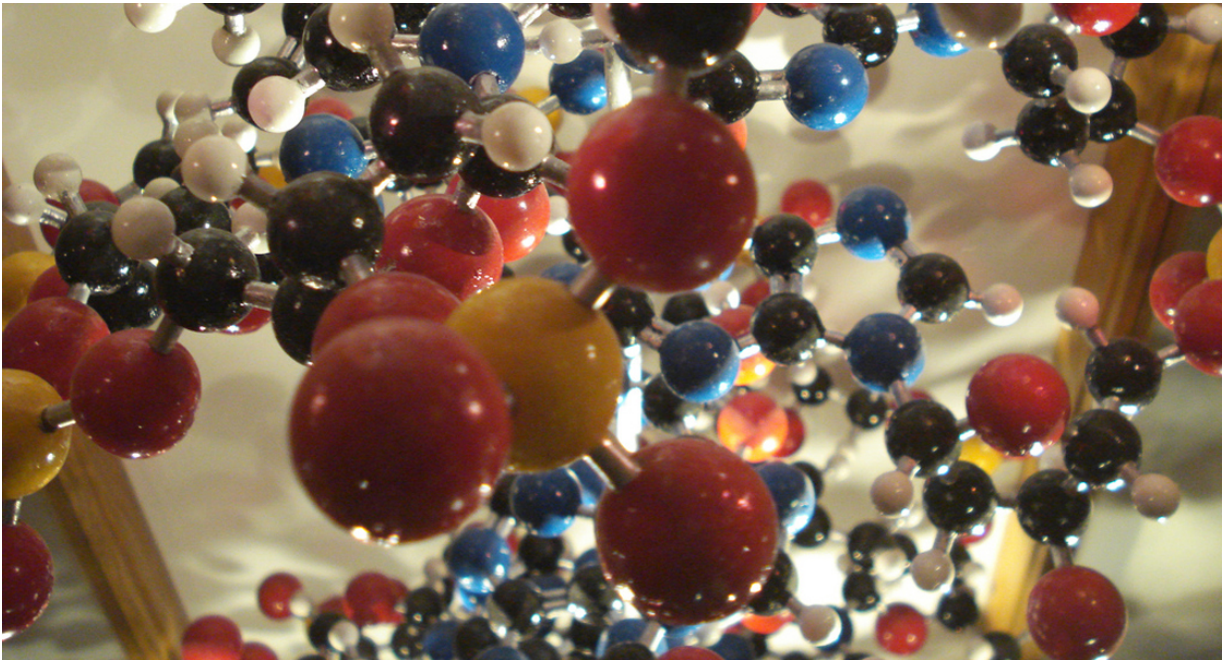
class="introduction"

Atoms are
the building
blocks of
molecules
found in the
universe—
air, soil,
water, rocks
. . . and also
the cells of
all living
organisms.

In this
model of an
organic
molecule,
the atoms of
carbon
(black),
hydrogen
(white),
nitrogen
(blue),
oxygen
(red), and
sulfur
(yellow) are
shown in
proportional
atomic size.

The silver
rods
indicate
chemical

bonds.
(credit:
modification
n of work
by Christian
Guthier)



Elements in various combinations comprise all matter, including living things. Some of the most abundant elements in living organisms include carbon, hydrogen, nitrogen, oxygen, sulfur, and phosphorus. These form the nucleic acids, proteins, carbohydrates, and lipids that are the fundamental components of living matter. Biologists must understand these important building blocks and the unique structures of the atoms that make up molecules, allowing for the formation of cells, tissues, organ systems, and entire organisms.

All biological processes follow the laws of physics and chemistry, so in order to understand how biological systems work, it is important to understand the underlying physics and chemistry. For example, the flow of blood within the circulatory system follows the laws of physics that regulate the modes of fluid flow. The breakdown of the large, complex molecules of

food into smaller molecules—and the conversion of these to release energy to be stored in adenosine triphosphate (ATP)—is a series of chemical reactions that follow chemical laws. The properties of water and the formation of hydrogen bonds are key to understanding living processes. Recognizing the properties of acids and bases is important, for example, to our understanding of the digestive process. Therefore, the fundamentals of physics and chemistry are important for gaining insight into biological processes.

Bis2A 02.1 Atoms, Isotopes, Ions, and Molecules: The Building Blocks

By the end of this section, you will be able to:

- Define matter and elements
- Describe the interrelationship between protons, neutrons, and electrons
- Compare the ways in which electrons can be donated or shared between atoms
- Explain the ways in which naturally occurring elements combine to create molecules, cells, tissues, organ systems, and organisms

At its most fundamental level, life is made up of matter. **Matter** is any substance that occupies space and has mass. **Elements** are unique forms of matter with specific chemical and physical properties that cannot be broken down into smaller substances by ordinary chemical reactions. There are 118 elements, but only 92 occur naturally. The remaining elements are synthesized in laboratories and are unstable.

Each element is designated by its chemical symbol, which is a single capital letter or, when the first letter is already “taken” by another element, a combination of two letters. Some elements follow the English term for the element, such as C for carbon and Ca for calcium. Other elements’ chemical symbols derive from their Latin names; for example, the symbol for sodium is Na, referring to *natrium*, the Latin word for sodium.

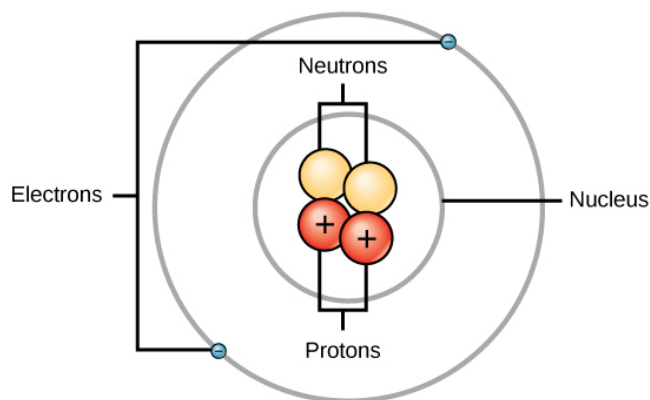
The four elements common to all living organisms are oxygen (O), carbon (C), hydrogen (H), and nitrogen (N). In the non-living world, elements are found in different proportions, and some elements common to living organisms are relatively rare on the earth as a whole, as shown in [\[link\]](#). For example, the atmosphere is rich in nitrogen and oxygen but contains little carbon and hydrogen, while the earth’s crust, although it contains oxygen and a small amount of hydrogen, has little nitrogen and carbon. In spite of their differences in abundance, all elements and the chemical reactions between them obey the same chemical and physical laws regardless of whether they are a part of the living or non-living world.

Approximate Percentage of Elements in Living Organisms (Humans) Compared to the Non-living World			
Element	Life (Humans)	Atmosphere	Earth's Crust
Oxygen (O)	65%	21%	46%
Carbon (C)	18%	trace	trace
Hydrogen (H)	10%	trace	0.1%
Nitrogen (N)	3%	78%	trace

The Structure of the Atom

To understand how elements come together, we must first discuss the smallest component or building block of an element, the atom. An **atom** is the smallest unit of matter that retains all of the chemical properties of an element. For example, one gold atom has all of the properties of gold in that it is a solid metal at room temperature. A gold coin is simply a very large number of gold atoms molded into the shape of a coin and containing small amounts of other elements known as impurities. Gold atoms cannot be broken down into anything smaller while still retaining the properties of gold.

An atom is composed of two regions: the **nucleus**, which is in the center of the atom and contains protons and neutrons, and the outermost region of the atom which holds its electrons in orbit around the nucleus, as illustrated in [\[link\]](#). Atoms contain protons, electrons, and neutrons, among other subatomic particles. The only exception is hydrogen (H), which is made of one proton and one electron with no neutrons.



Elements, such as helium, depicted here, are made up of atoms. Atoms are made up of protons and neutrons located within the nucleus, with electrons in orbitals surrounding the nucleus.

Protons and neutrons have approximately the same mass, about 1.67×10^{-24} grams. Scientists arbitrarily define this amount of mass as one atomic mass unit (amu) or one Dalton, as shown in [\[link\]](#). Although similar in mass, protons and neutrons differ in their electric charge. A **proton** is positively charged whereas a **neutron** is uncharged. Therefore, the number of neutrons in an atom contributes significantly to its mass, but not to its charge. **Electrons** are much smaller in mass than protons, weighing only 9.11×10^{-28} grams, or about 1/1800 of an atomic mass unit. Hence, they do not contribute much to an element's overall atomic mass. Therefore, when considering atomic mass, it is customary to ignore the mass of any electrons and calculate the atom's mass based on the number of protons and neutrons alone. Although not significant contributors to mass, electrons do contribute greatly to the atom's charge, as each electron has a negative charge equal to the positive charge of a proton. In uncharged, neutral atoms, the number of electrons orbiting the nucleus is equal to the number of protons inside the nucleus. In these atoms, the positive and negative charges cancel each other out, leading to an atom with no net charge.

Accounting for the sizes of protons, neutrons, and electrons, most of the volume of an atom—greater than 99 percent—is, in fact, empty space. With all this empty space, one might ask why so-called solid objects do not just pass through one another. The reason they do not is that the electrons that surround all atoms are negatively charged and negative charges repel each other.

Protons, Neutrons, and Electrons			
	Charge	Mass (amu)	Location
Proton	+1	1	nucleus
Neutron	0	1	nucleus
Electron	−1	0	orbitals

Video clips

For a review of atomic structure check out this You-tube video: [atomic structure](#).

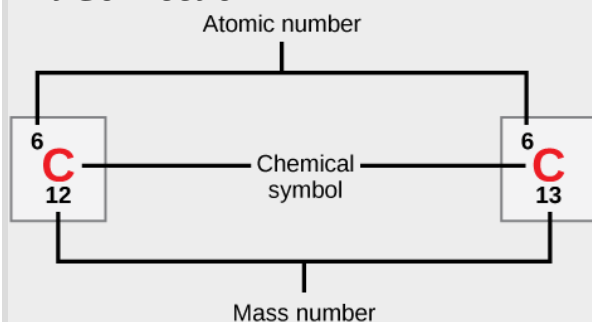
Atomic Number and Mass

Atoms of each element contain a characteristic number of protons and electrons. The number of protons determines an element's **atomic number** and is used to distinguish one element from another. The number of neutrons is variable, resulting in isotopes, which are different forms of the same atom that vary only in the number of neutrons they possess. Together, the number of protons and the number of neutrons determine an element's **mass number**, as illustrated in [\[link\]](#). Note that the small contribution of mass from electrons is disregarded in calculating the mass number. This approximation of mass can be used to easily calculate how many neutrons

an element has by simply subtracting the number of protons from the mass number. Since an element's isotopes will have slightly different mass numbers, scientists also determine the **atomic mass**, which is the calculated mean of the mass number for its naturally occurring isotopes. Often, the resulting number contains a fraction. For example, the atomic mass of chlorine (Cl) is 35.45 because chlorine is composed of several isotopes, some (the majority) with atomic mass 35 (17 protons and 18 neutrons) and some with atomic mass 37 (17 protons and 20 neutrons).

Note:

Art Connection



Carbon has an atomic number of six, and two stable isotopes with mass numbers of twelve and thirteen, respectively. Its atomic mass is 12.11.

How many neutrons do carbon-12 and carbon-13 have, respectively?

Isotopes

Isotopes are different forms of an element that have the same number of protons but a different number of neutrons. Some elements—such as carbon, potassium, and uranium—have naturally occurring isotopes.

Carbon-12 contains six protons, six neutrons, and six electrons; therefore, it has a mass number of 12 (six protons and six neutrons). Carbon-14 contains six protons, eight neutrons, and six electrons; its atomic mass is 14 (six protons and eight neutrons). These two alternate forms of carbon are isotopes. Some isotopes may emit neutrons, protons, and electrons, and attain a more stable atomic configuration (lower level of potential energy); these are radioactive isotopes, or **radioisotopes**. Radioactive decay (carbon-14 losing neutrons to eventually become carbon-12) describes the energy loss that occurs when an unstable atom's nucleus releases radiation.

Note:

Evolution Connection

Carbon Dating

Carbon is normally present in the atmosphere in the form of gaseous compounds like carbon dioxide and methane. Carbon-14 (^{14}C) is a naturally occurring radioisotope that is created in the atmosphere from atmospheric ^{14}N (nitrogen) by the addition of a neutron and the loss of a proton because of cosmic rays. This is a continuous process, so more ^{14}C is always being created. As a living organism incorporates ^{14}C initially as carbon dioxide fixed in the process of photosynthesis, the relative amount of ^{14}C in its body is equal to the concentration of ^{14}C in the atmosphere. When an organism dies, it is no longer ingesting ^{14}C , so the ratio between ^{14}C and ^{12}C will decline as ^{14}C decays gradually to ^{14}N by a process called beta decay—the emission of electrons or positrons. This decay gives off energy in a slow process.

After approximately 5,730 years, half of the starting concentration of ^{14}C will have been converted back to ^{14}N . The time it takes for half of the original concentration of an isotope to decay back to its more stable form is called its half-life. Because the half-life of ^{14}C is long, it is used to date formerly living objects such as old bones or wood. Comparing the ratio of the ^{14}C concentration found in an object to the amount of ^{14}C detected in the atmosphere, the amount of the isotope that has not yet decayed can be determined. On the basis of this amount, the age of the material, such as the pygmy mammoth shown in [\[link\]](#), can be calculated with accuracy if it is not much older than about 50,000 years. Other elements have isotopes

with different half lives. For example, ^{40}K (potassium-40) has a half-life of 1.25 billion years, and ^{235}U (Uranium 235) has a half-life of about 700 million years. Through the use of radiometric dating, scientists can study the age of fossils or other remains of extinct organisms to understand how organisms have evolved from earlier species.



The age of carbon-containing remains less than about 50,000 years old, such as this pygmy mammoth, can be determined using carbon dating. (credit: Bill Faulkner, NPS)

Note:

Link to Learning



To learn more about atoms, isotopes, and how to tell one isotope from another, visit [this site](#) and run the simulation.

The Periodic Table

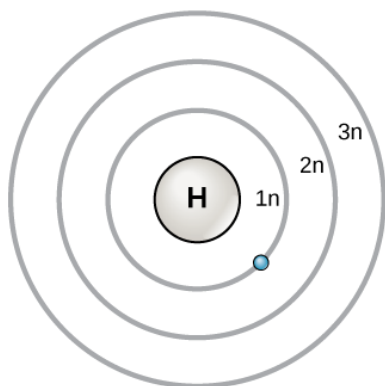
The different elements are organized and displayed in the **periodic table**. Devised by Russian chemist Dmitri Mendeleev (1834–1907) in 1869, the table groups elements that, although unique, share certain chemical properties with other elements. The properties of elements are responsible for their physical state at room temperature: they may be gases, solids, or liquids. Elements also have specific **chemical reactivity**, the ability to combine and to chemically bond with each other.

In the periodic table, shown in [\[link\]](#), the elements are organized and displayed according to their atomic number and are arranged in a series of rows and columns based on shared chemical and physical properties. In addition to providing the atomic number for each element, the periodic table also displays the element's atomic mass. Looking at carbon, for example, its symbol (C) and name appear, as well as its atomic number of six (in the upper left-hand corner) and its atomic mass of 12.11.

Electron Shells and the Bohr Model

It should be stressed that there is a connection between the number of protons in an element, the atomic number that distinguishes one element from another, and the number of electrons it has. In all electrically neutral atoms, the number of electrons is the same as the number of protons. Thus, each element, at least when electrically neutral, has a characteristic number of electrons equal to its atomic number.

An early model of the atom was developed in 1913 by Danish scientist Niels Bohr (1885–1962). The Bohr model shows the atom as a central nucleus containing protons and neutrons, with the electrons in circular **orbitals** at specific distances from the nucleus, as illustrated in [\[link\]](#). These orbits form electron shells or energy levels, which are a way of visualizing the number of electrons in the outermost shells. These energy levels are designated by a number and the symbol “n.” For example, 1n represents the first energy level located closest to the nucleus.



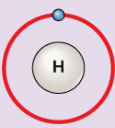
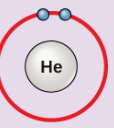
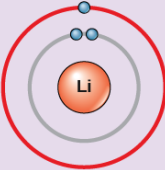
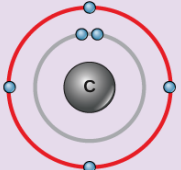
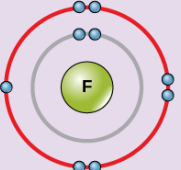
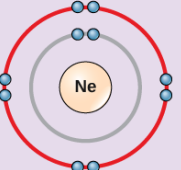
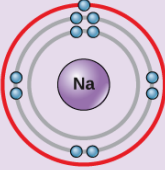
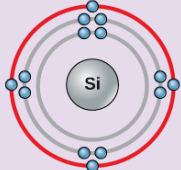
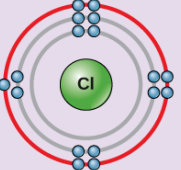
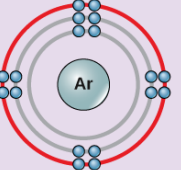
The Bohr model was developed by Niels Bohrs in 1913. In this model, electrons exist within principal shells. An electron normally exists

in the lowest energy shell available, which is the one closest to the nucleus. Energy from a photon of light can bump it up to a higher energy shell, but this situation is unstable, and the electron quickly decays back to the ground state. In the process, a photon of light is released.

Electrons fill orbitals in a consistent order: they first fill the orbitals closest to the nucleus, then they continue to fill orbitals of increasing energy further from the nucleus. If there are multiple orbitals of equal energy, they will be filled with one electron in each energy level before a second electron is added. The electrons of the outermost energy level determine the energetic stability of the atom and its tendency to form chemical bonds with other atoms to form molecules.

Under standard conditions, atoms fill the inner shells first, often resulting in a variable number of electrons in the outermost shell. The innermost shell has a maximum of two electrons but the next two electron shells can each have a maximum of eight electrons. This is known as the **octet rule**, which states, with the exception of the innermost shell, that atoms are more stable energetically when they have eight electrons in their **valence shell**, the outermost electron shell. Examples of some neutral atoms and their electron configurations are shown in [\[link\]](#). Notice that in this [\[link\]](#), helium has a complete outer electron shell, with two electrons filling its first and only shell. Similarly, neon has a complete outer 2n shell containing eight electrons. In contrast, chlorine and sodium have seven and one in their outer shells, respectively, but theoretically they would be more energetically stable if they followed the octet rule and had eight.

Note:**Art Connection**

	Group 1	Group 14	Group 17	Group 18
Period 1 (1n is filling)				
Period 2 (2n is filling)				
Period 3 (3n is filling)				

Bohr diagrams indicate how many electrons fill each principal shell. Group 18 elements (helium, neon, and argon are shown) have a full outer, or valence, shell. A full valence shell is the most stable electron configuration. Elements in other groups have partially filled valence shells and gain or lose electrons to achieve a stable electron configuration.

An atom may give, take, or share electrons with another atom to achieve a full valence shell, the most stable electron configuration. Looking at this figure, how many electrons do elements in group 1 need to lose in order to achieve a stable electron configuration? How many electrons do elements in groups 14 and 17 need to gain to achieve a stable configuration?

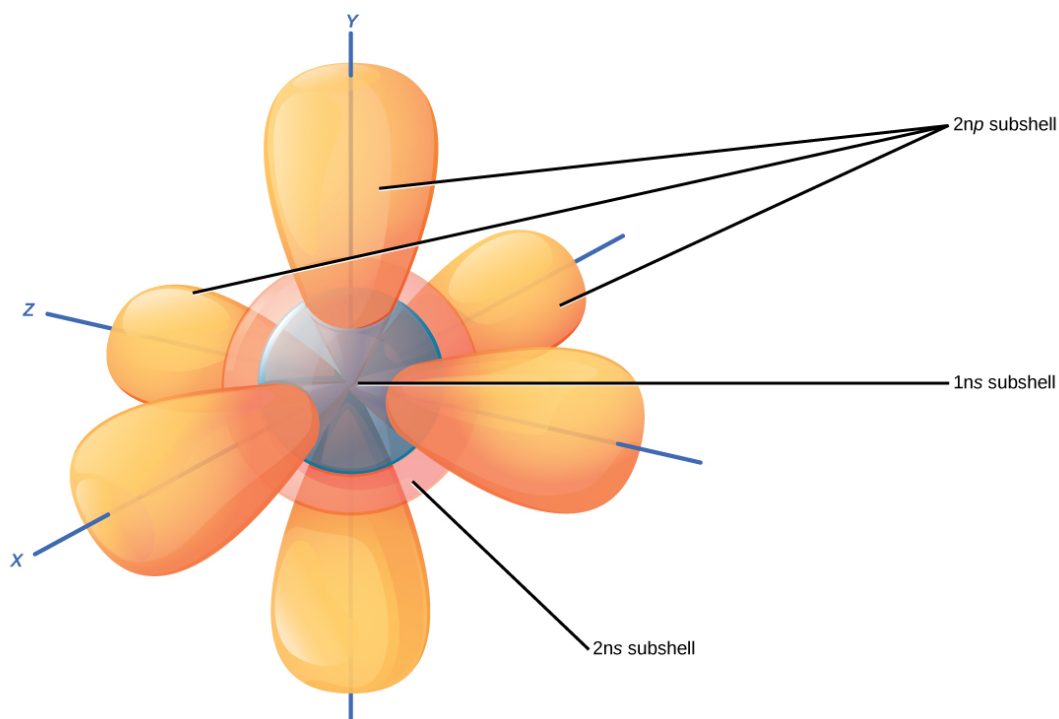
Understanding that the organization of the periodic table is based on the total number of protons (and electrons) helps us know how electrons are distributed among the outer shell. The periodic table is arranged in columns

and rows based on the number of electrons and where these electrons are located. Take a closer look at the some of the elements in the table's far right column in [\[link\]](#). The group 18 atoms helium (He), neon (Ne), and argon (Ar) all have filled outer electron shells, making it unnecessary for them to share electrons with other atoms to attain stability; they are highly stable as single atoms. Their non-reactivity has resulted in their being named the **inert gases** (or **noble gases**). Compare this to the group 1 elements in the left-hand column. These elements, including hydrogen (H), lithium (Li), and sodium (Na), all have one electron in their outermost shells. That means that they can achieve a stable configuration and a filled outer shell by donating or sharing one electron with another atom or a molecule such as water. Hydrogen will donate or share its electron to achieve this configuration, while lithium and sodium will donate their electron to become stable. As a result of losing a negatively charged electron, they become positively charged **ions**. Group 17 elements, including fluorine and chlorine, have seven electrons in their outmost shells, so they tend to fill this shell with an electron from other atoms or molecules, making them negatively charged ions. Group 14 elements, of which carbon is the most important to living systems, have four electrons in their outer shell allowing them to make several covalent bonds (discussed below) with other atoms. Thus, the columns of the periodic table represent the potential shared state of these elements' outer electron shells that is responsible for their similar chemical characteristics.

Electron Orbitals

Although useful to explain the reactivity and chemical bonding of certain elements, the Bohr model of the atom does not accurately reflect how electrons are spatially distributed surrounding the nucleus. They do not circle the nucleus like the earth orbits the sun, but are found in **electron orbitals**. These relatively complex shapes result from the fact that electrons behave not just like particles, but also like waves. Mathematical equations from quantum mechanics known as wave functions can predict within a certain level of probability where an electron might be at any given time. The area where an electron is most likely to be found is called its orbital.

Recall that the Bohr model depicts an atom's electron shell configuration. Within each electron shell are subshells, and each subshell has a specified number of orbitals containing electrons. While it is impossible to calculate exactly where an electron is located, scientists know that it is most probably located within its orbital path. Subshells are designated by the letter *s*, *p*, *d*, and *f*. The *s* subshell is spherical in shape and has one orbital. Principal shell $1n$ has only a single *s* orbital, which can hold two electrons. Principal shell $2n$ has one *s* and one *p* subshell, and can hold a total of eight electrons. The *p* subshell has three dumbbell-shaped orbitals, as illustrated in [\[link\]](#). Subshells *d* and *f* have more complex shapes and contain five and seven orbitals, respectively. These are not shown in the illustration. Principal shell $3n$ has *s*, *p*, and *d* subshells and can hold 18 electrons. Principal shell $4n$ has *s*, *p*, *d* and *f* orbitals and can hold 32 electrons. Moving away from the nucleus, the number of electrons and orbitals found in the energy levels increases. Progressing from one atom to the next in the periodic table, the electron structure can be worked out by fitting an extra electron into the next available orbital.



The *s* subshells are shaped like spheres. Both the $1n$ and $2n$

principal shells have an *s* orbital, but the size of the sphere is larger in the $2n$ orbital. Each sphere is a single orbital. *p* subshells are made up of three dumbbell-shaped orbitals. Principal shell $2n$ has a *p* subshell, but shell 1 does not.

The closest orbital to the nucleus, called the $1s$ orbital, can hold up to two electrons. This orbital is equivalent to the innermost electron shell of the Bohr model of the atom. It is called the $1s$ orbital because it is spherical around the nucleus. The $1s$ orbital is the closest orbital to the nucleus, and it is always filled first, before any other orbital can be filled. Hydrogen has one electron; therefore, it has only one spot within the $1s$ orbital occupied. This is designated as $1s^1$, where the superscripted 1 refers to the one electron within the $1s$ orbital. Helium has two electrons; therefore, it can completely fill the $1s$ orbital with its two electrons. This is designated as $1s^2$, referring to the two electrons of helium in the $1s$ orbital. On the periodic table [\[link\]](#), hydrogen and helium are the only two elements in the first row (period); this is because they only have electrons in their first shell, the $1s$ orbital. Hydrogen and helium are the only two elements that have the $1s$ and no other electron orbitals in the electrically neutral state.

The second electron shell may contain eight electrons. This shell contains another spherical *s* orbital and three “dumbbell” shaped *p* orbitals, each of which can hold two electrons, as shown in [\[link\]](#). After the $1s$ orbital is filled, the second electron shell is filled, first filling its $2s$ orbital and then its three *p* orbitals. When filling the *p* orbitals, each takes a single electron; once each *p* orbital has an electron, a second may be added. Lithium (Li) contains three electrons that occupy the first and second shells. Two electrons fill the $1s$ orbital, and the third electron then fills the $2s$ orbital. Its **electron configuration** is $1s^2 2s^1$. Neon (Ne), on the other hand, has a total of ten electrons: two are in its innermost $1s$ orbital and eight fill its second shell (two each in the $2s$ and three *p* orbitals); thus, it is an inert gas and energetically stable as a single atom that will rarely form a chemical bond with other atoms. Larger elements have additional orbitals, making up the third electron shell. While the concepts of electron shells and orbitals are closely related, orbitals provide a more accurate depiction of the electron

configuration of an atom because the orbital model specifies the different shapes and special orientations of all the places that electrons may occupy.

video clip

[Electron Orbital](#) animation.

Note:

Link to Learning



Watch [this visual animation](#) to see the spatial arrangement of the p and s orbitals.

Exercise:

A quick question

Problem:

Potassium has an atomic number of 19. What is its electron configuration?

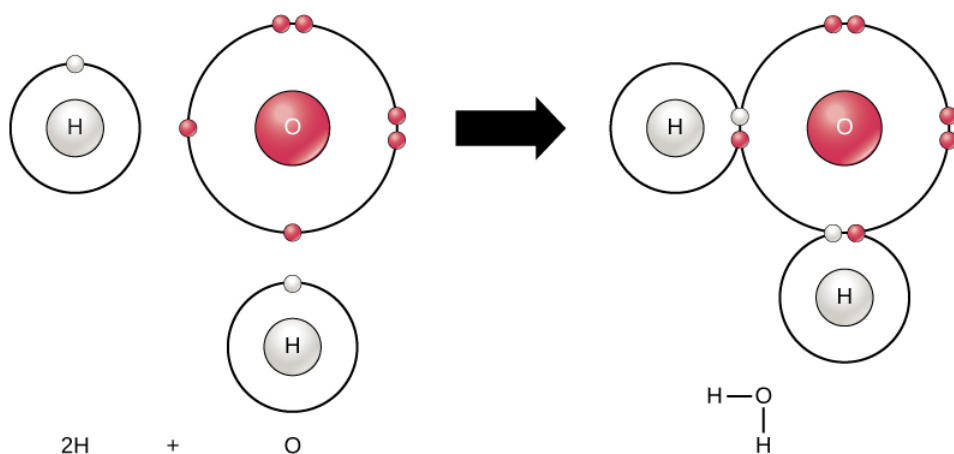
- a. shells 1 and 2 are full, and shell 3 has nine electrons
- b. shells 1, 2 and 3 are full and shell 4 has three electrons
- c. shells 1, 2 and 3 are full and shell 4 has one electron
- d. shells 1, 2 and 3 are full and no other electrons are present

Solution:

C

Chemical Reactions and Molecules

All elements are most stable when their outermost shell is filled with electrons according to the octet rule. This is because it is energetically favorable for atoms to be in that configuration and it makes them stable. However, since not all elements have enough electrons to fill their outermost shells, atoms form **chemical bonds** with other atoms thereby obtaining the electrons they need to attain a stable electron configuration. When two or more atoms chemically bond with each other, the resultant chemical structure is a molecule. The familiar water molecule, H_2O , consists of two hydrogen atoms and one oxygen atom; these bond together to form water, as illustrated in [\[link\]](#). Atoms can form molecules by donating, accepting, or sharing electrons to fill their outer shells.

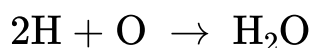


Two or more atoms may bond with each other to form a molecule. When two hydrogens and an oxygen share electrons via covalent bonds, a water molecule is formed.

Chemical reactions occur when two or more atoms bond together to form molecules or when bonded atoms are broken apart. The substances used in

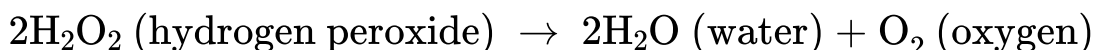
the beginning of a chemical reaction are called the **reactants** (usually found on the left side of a chemical equation), and the substances found at the end of the reaction are known as the **products** (usually found on the right side of a chemical equation). An arrow is typically drawn between the reactants and products to indicate the direction of the chemical reaction; this direction is not always a “one-way street.” For the creation of the water molecule shown above, the chemical equation would be:

Equation:

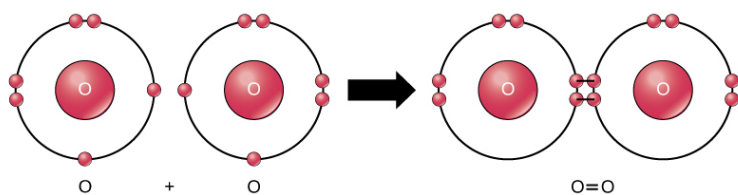


An example of a simple chemical reaction is the breaking down of hydrogen peroxide molecules, each of which consists of two hydrogen atoms bonded to two oxygen atoms (H_2O_2). The reactant hydrogen peroxide is broken down into water, containing one oxygen atom bound to two hydrogen atoms (H_2O), and oxygen, which consists of two bonded oxygen atoms (O_2). In the equation below, the reaction includes two hydrogen peroxide molecules and two water molecules. This is an example of a **balanced chemical equation**, wherein the number of atoms of each element is the same on each side of the equation. According to the law of conservation of matter, the number of atoms before and after a chemical reaction should be equal, such that no atoms are, under normal circumstances, created or destroyed.

Equation:



Even though all of the reactants and products of this reaction are molecules (each atom remains bonded to at least one other atom), in this reaction only hydrogen peroxide and water are representatives of **compounds**: they contain atoms of more than one type of element. Molecular oxygen, on the other hand, as shown in [\[link\]](#), consists of two doubly bonded oxygen atoms and is not classified as a compound but as a mononuclear molecule.



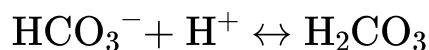
The oxygen atoms in an O_2 molecule are joined by a double bond.

Some chemical reactions, such as the one shown above, can proceed in one direction until the reactants are all used up. The equations that describe these reactions contain a unidirectional arrow and are **irreversible**.

Reversible reactions are those that can go in either direction. In reversible reactions, reactants are turned into products, but when the concentration of product goes beyond a certain threshold (characteristic of the particular reaction), some of these products will be converted back into reactants; at this point, the designations of products and reactants are reversed. This back and forth continues until a certain relative balance between reactants and products occurs—a state called **equilibrium**. These situations of reversible reactions are often denoted by a chemical equation with a double headed arrow pointing towards both the reactants and products.

For example, in human blood, excess hydrogen ions (H^+) bind to bicarbonate ions (HCO_3^-) forming an equilibrium state with carbonic acid (H_2CO_3). If carbonic acid were added to this system, some of it would be converted to bicarbonate and hydrogen ions.

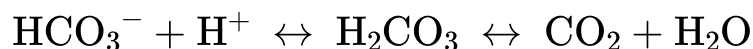
Equation:



In biological reactions, however, equilibrium is rarely obtained because the concentrations of the reactants or products or both are constantly changing, often with a product of one reaction being a reactant for another. To return to the example of excess hydrogen ions in the blood, the formation of carbonic acid will be the major direction of the reaction. However, the

carbonic acid can also leave the body as carbon dioxide gas (via exhalation) instead of being converted back to bicarbonate ion, thus driving the reaction to the right by the chemical law known as **law of mass action**. These reactions are important for maintaining the homeostasis of our blood.

Equation:



Exercise:

Reading a chemical reaction

Problem:

$\text{C}_6\text{H}_{12}\text{O}_6 + \text{O}_2 \rightarrow \text{CO}_2 + \text{H}_2\text{O}$ Using this equation, which of the following are the reactants?

- a. $\text{C}_6\text{H}_{12}\text{O}_6$
- b. CO_2
- c. H_2O
- d. O_2
- e. both A and B
- f. both A and D
- g. all of the above

Solution:

f

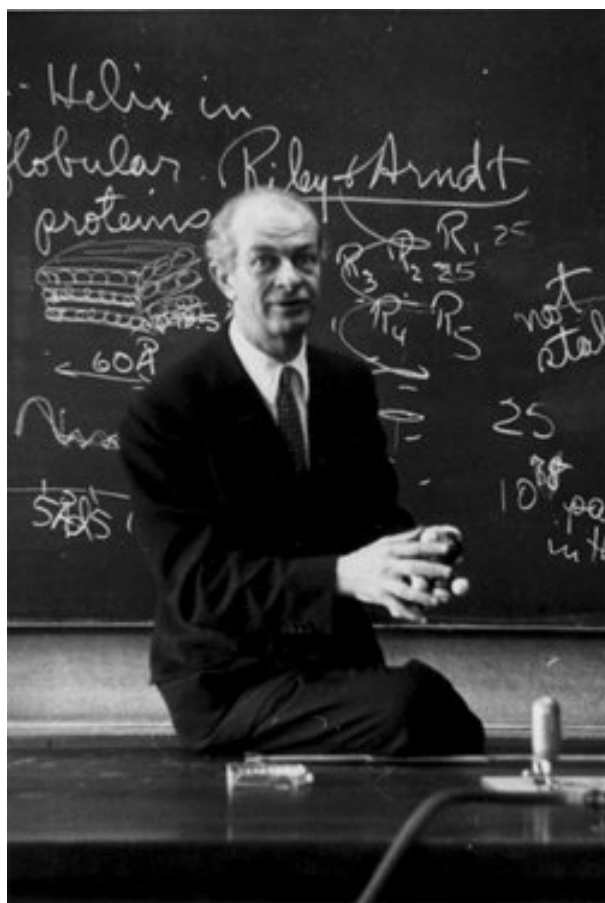
Exercise 2: Reading a chemical reaction

What else can you say about the reaction above? What are the products? Is the reaction reversible? what compound does $\text{C}_6\text{H}_{12}\text{O}_6$ stand for? In class you will be asked to describe simple and complicated chemical reactions. Be sure to practice this skill with your classmates.

Electronegativity

An issue with ionization potential and electron affinity is that they are defined and measured as reactions in the gas phase. Although values have been determined for molecular fragments it is still difficult to correlate with reaction trends in solution. To overcome this issue the concept of electronegativity was developed.

Electronegativity is defined as the *tendency of an atom in a molecule to attract electrons to itself*. Although several electronegativity scales have been developed, that by Linus Pauling ([\[link\]](#)) is the most often used. [\[link\]](#) provides selected Pauling electronegativity values (unit less).



American chemist Linus Carl Pauling (1901 –1994).

Element	Pauling scale
F	4.0
O	3.5
Cl	3.0
N	3.0
S	2.5
C	2.5
H	2.1
B	2.0
Na	0.9

Selected Pauling electronegativity values.

The advantage of the Pauling electronegativity scale is that it allows the prediction of general behavior. When comparing electronegativity values between two atoms, the larger the value, the stronger the "pull" on the electrons and the more "ionic character" the interaction or bond will possess. For example, let's compare the electronegativity of O (3.5) and H (2.1). Because O has a higher electronegativity, O will tend to "pull" the electrons from H, this gives rise to a slight but significant negative charge around the O atom due to the higher tendency of the electrons to be associated with the O atom. It therefore gives a slight positive charge to the H atom due to the decrease in the probability of finding an electron near by. It is electronegativity, the tendency to attract electrons that gives rise to the concept of **polarity** and **dipole**. Thus, a H-O bond ($3.5 - 2.1 = 1.4$) is more polar than a H-S bond ($2.5 - 2.1 = 0.4$).

Finally, we can use the periodic table to get a general idea as to the strength or weakness of an atoms electronegativity. Those atoms with the strongest electronegativity tend to reside int he upper right hand corner of the table, such as fluorine (F), oxygen (O) and Chlorine (Cl); while the lowest electronegativity tend to be found at the other end of the table, in the lower left, such as francium (Fr, 0.7), cesium (Cs, 0.79) and radium (Ra, 0.89). More information on electronegativity can be found at the UC Davis chemwiki site: [UC Davis Chemwiki Electronegativity](#).

Exercise:

Periodic Table and Electronegativity

Problem: Using a periodic table, electronegativity increases as

- a. you move from the top of the tower to the bottom
- b. you move from the bottom to the top
- c. as you move from the bottom to the top, from left to right
- d. as you move from the top to the bottom, from right to left
- e. none of the above

Solution:

c

Exercise:

Periodic Table and Electronegativity

Problem:

Using a periodic table, rank the following atoms from most to least electronegative: N, P, O, F

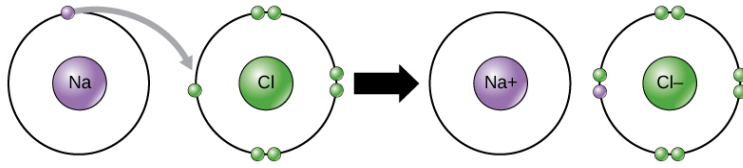
- a. N, P, O, F
- b. F, O, P, N
- c. F, O, N, P

Solution:

Ions and Ionic Bonds

Some atoms are more stable when they gain or lose an electron (or possibly two) and form ions. This fills their outermost electron shell and makes them energetically more stable. Because the number of electrons does not equal the number of protons, each ion has a net charge. **Cations** are positive ions that are formed by losing electrons. Negative ions are formed by gaining electrons and are called anions. **Anions** are designated by their elemental name being altered to end in “-ide”: the anion of chlorine is called chloride, and the anion of sulfur is called sulfide, for example.

This movement of electrons from one element to another is referred to as **electron transfer**. As [\[link\]](#) illustrates, sodium (Na) only has one electron in its outer electron shell. It takes less energy for sodium to donate that one electron than it does to accept seven more electrons to fill the outer shell. If sodium loses an electron, it now has 11 protons, 11 neutrons, and only 10 electrons, leaving it with an overall charge of +1. It is now referred to as a sodium ion. Chlorine (Cl) in its lowest energy state (called the ground state) has seven electrons in its outer shell. Again, it is more energy-efficient for chlorine to gain one electron than to lose seven. Therefore, it tends to gain an electron to create an ion with 17 protons, 17 neutrons, and 18 electrons, giving it a net negative (−1) charge. It is now referred to as a chloride ion. In this example, sodium will donate its one electron to empty its shell, and chlorine will accept that electron to fill its shell. Both ions now satisfy the octet rule and have complete outermost shells. Because the number of electrons is no longer equal to the number of protons, each is now an ion and has a +1 (sodium cation) or −1 (chloride anion) charge. Note that these transactions can normally only take place simultaneously: in order for a sodium atom to lose an electron, it must be in the presence of a suitable recipient like a chlorine atom.



In the formation of an ionic compound, metals lose electrons and nonmetals gain electrons to achieve an octet.

Ionic bonds are formed between ions with opposite charges. For instance, positively charged sodium ions and negatively charged chloride ions bond together to make crystals of sodium chloride, or table salt, creating a crystalline molecule with zero net charge.

Certain salts are referred to in physiology as **electrolytes** (including sodium, potassium, and calcium), ions necessary for nerve impulse conduction, muscle contractions and water balance. Many sports drinks and dietary supplements provide these ions to replace those lost from the body via sweating during exercise.

So why are ionic bonds important in biology?

- They play an important role in determining the shapes (tertiary and quaternary structures) of proteins
- They are involved in the process of enzymic catalysis
- They are important in determining the shapes of chromosomes.
- They play a role in muscle contraction and cell shape.
- They are important in establishing polarized membranes for neuron function and muscle contraction.

Exercise:

Thought question

Problem:

Can you think of additional ways ionic bonding or ionic interactions are important in biological processes?

Solution:

This will be discussed in class

For additional information

Check out the link from the Khan academy on [ionic bonds](#).

Covalent Bonds and Other Bonds and Interactions

Another way the octet rule can be satisfied is by the sharing of electrons between atoms to form **covalent bonds**. These bonds are stronger and much more common than ionic bonds in the molecules of living organisms. Covalent bonds are commonly found in carbon-based organic molecules, such as our DNA and proteins. Covalent bonds are also found in inorganic molecules like H_2O , CO_2 , and O_2 . One, two, or three pairs of electrons may be shared, making single, double, and triple bonds, respectively. The more covalent bonds between two atoms, the stronger their connection. Thus, triple bonds are the strongest.

The strength of different levels of covalent bonding is one of the main reasons living organisms have a difficult time in acquiring nitrogen for use in constructing their molecules, even though molecular nitrogen, N_2 , is the most abundant gas in the atmosphere. Molecular nitrogen consists of two nitrogen atoms triple bonded to each other and, as with all molecules, the sharing of these three pairs of electrons between the two nitrogen atoms allows for the filling of their outer electron shells, making the molecule more stable than the individual nitrogen atoms. This strong triple bond makes it difficult for living systems to break apart this nitrogen in order to use it as constituents of proteins and DNA.

The formation of water molecules provides an example of covalent bonding. The hydrogen and oxygen atoms that combine to form water molecules are bound together by covalent bonds, as shown in [\[link\]](#). The electron from the hydrogen splits its time between the incomplete outer shell of the hydrogen atoms and the incomplete outer shell of the oxygen atoms. To completely fill the outer shell of oxygen, which has six electrons in its outer shell but which would be more stable with eight, two electrons

(one from each hydrogen atom) are needed: hence the well-known formula H_2O . The electrons are shared between the two elements to fill the outer shell of each, making both elements more stable.

Note:

Link to Learning



View [this short video](#) to see an animation of ionic and covalent bonding.

Polar Covalent Bonds

There are two types of covalent bonds: polar and nonpolar. In a **polar covalent bond**, shown in [\[link\]](#), the electrons are unequally shared by the atoms and are attracted more to one nucleus than the other. Because of the unequal distribution of electrons between the atoms of different elements, a slightly positive ($\delta+$) or slightly negative ($\delta-$) charge develops. This partial charge is an important property of water and accounts for many of its characteristics.

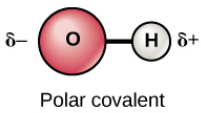
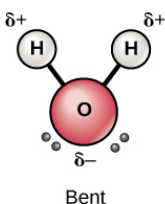
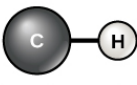
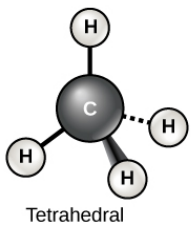
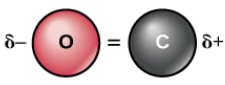
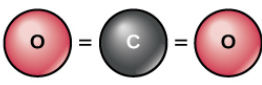
Water is a polar molecule, with the hydrogen atoms acquiring a partial positive charge and the oxygen a partial negative charge. This occurs because the nucleus of the oxygen atom is more attractive to the electrons of the hydrogen atoms than the hydrogen nucleus is to the oxygen's electrons. Thus oxygen has a higher **electronegativity** than hydrogen and the shared electrons spend more time in the vicinity of the oxygen nucleus than they do near the nucleus of the hydrogen atoms, giving the atoms of oxygen and hydrogen slightly negative and positive charges, respectively. Another way of stating this is that the probability of finding a shared

electron near an oxygen nucleus is more likely than finding it near a hydrogen nucleus. Either way, the atom's relative electronegativity contributes to the development of partial charges whenever one element is significantly more electronegative than the other, and the charges generated by these polar bonds may then be used for the formation of hydrogen bonds based on the attraction of opposite partial charges. (Hydrogen bonds, which are discussed in detail below, are weak bonds between slightly positively charged hydrogen atoms to slightly negatively charged atoms in other molecules.) Since macromolecules often have atoms within them that differ in electronegativity, polar bonds are often present in organic molecules.

Nonpolar Covalent Bonds

Nonpolar covalent bonds form between two atoms of the same element or between different elements that share electrons equally. For example, molecular oxygen (O_2) is nonpolar because the electrons will be equally distributed between the two oxygen atoms.

Another example of a nonpolar covalent bond is methane (CH_4), also shown in [\[link\]](#). Carbon has four electrons in its outermost shell and needs four more to fill it. It gets these four from four hydrogen atoms, each atom providing one, making a stable outer shell of eight electrons. Carbon and hydrogen do not have the same electronegativity but are similar; thus, nonpolar bonds form. The hydrogen atoms each need one electron for their outermost shell, which is filled when it contains two electrons. These elements share the electrons equally among the carbons and the hydrogen atoms, creating a nonpolar covalent molecule.

	Bond type	Molecular shape	Molecular type
Water	 Polar covalent	 Bent	Polar
Methane	 Nonpolar covalent	 Tetrahedral	Nonpolar
Carbon dioxide	 Polar covalent	 Linear	Nonpolar

Whether a molecule is polar or nonpolar depends both on bond type and molecular shape. Both water and carbon dioxide have polar covalent bonds, but carbon dioxide is linear, so the partial charges on the molecule cancel each other out.

Hydrogen Bonds and Van Der Waals Interactions

Ionic and covalent bonds between elements require energy to break. Ionic bonds are not as strong as covalent, which determines their behavior in biological systems. However, not all bonds are ionic or covalent bonds. Weaker bonds can also form between molecules. Two weak bonds that occur frequently are hydrogen bonds and van der Waals interactions. Without these two types of bonds, life as we know it would not exist. Hydrogen bonds provide many of the critical, life-sustaining properties of

water and also stabilize the structures of proteins and DNA, the building block of cells.

When polar covalent bonds containing hydrogen form, the hydrogen in that bond has a slightly positive charge because hydrogen's electron is pulled more strongly toward the other element and away from the hydrogen. Because the hydrogen is slightly positive, it will be attracted to neighboring negative charges. When this happens, a weak interaction occurs between the δ^+ of the hydrogen from one molecule and the δ^- charge on the more electronegative atoms of another molecule, usually oxygen or nitrogen, or within the same molecule. This interaction is called a **hydrogen bond**. This type of bond is common and occurs regularly between water molecules. Individual hydrogen bonds are weak and easily broken; however, they occur in very large numbers in water and in organic polymers, creating a major force in combination. Hydrogen bonds are also responsible for zipping together the DNA double helix.

Like hydrogen bonds, **van der Waals interactions** are weak attractions or interactions between molecules. Van der Waals attractions can occur between any two or more molecules and are dependent on slight fluctuations of the electron densities, which are not always symmetrical around an atom. For these attractions to happen, the molecules need to be very close to one another. These bonds—along with ionic, covalent, and hydrogen bonds—contribute to the three-dimensional structure of the proteins in our cells that is necessary for their proper function.

For Additional Information

Khan Academy Links

For more information here are some video links from the Khan Academy. To view videos from the Khan Academy you will need to sign up and register. You can sign up at [Khan Academy](#). These may prove helpful if you are still having trouble with some of the basic concepts.

- [Periodic Table](#)
- [Introduction to the Atom](#)
- [Orbitals and electrons](#)

ChemWiki Sites

Many of these basic concepts can also be found at the UC Davis Chemwiki site. We will provide links to various topics that you can further explore at Chemwiki. Below are some specific sites that may be helpful if you are still having difficulty with these topics:

- [Electronic Configurations](#)
- [The Chemistry of Hydrogen](#)

Section Summary

Matter is anything that occupies space and has mass. It is made up of elements. All of the 92 elements that occur naturally have unique qualities that allow them to combine in various ways to create molecules, which in turn combine to form cells, tissues, organ systems, and organisms. Atoms, which consist of protons, neutrons, and electrons, are the smallest units of an element that retain all of the properties of that element. Electrons can be transferred, shared, or cause charge disparities between atoms to create bonds, including ionic, covalent, and hydrogen bonds, as well as van der Waals interactions.

Art Connections

Exercise:

Problem:

[\[link\]](#) How many neutrons do carbon-12 and carbon-13 have, respectively?

Solution:

[\[link\]](#) Carbon-12 has six neutrons. Carbon-13 has seven neutrons.

Exercise:

Problem:

[\[link\]](#) An atom may give, take, or share electrons with another atom to achieve a full valence shell, the most stable electron configuration. Looking at this figure, how many electrons do elements in group 1 need to lose in order to achieve a stable electron configuration? How many electrons do elements in groups 14 and 17 need to gain to achieve a stable configuration?

Solution:

[\[link\]](#) Elements in group 1 need to lose one electron to achieve a stable electron configuration. Elements in groups 14 and 17 need to gain four and one electrons, respectively, to achieve a stable configuration.

Review Questions**Exercise:**

Problem: Which type of bond represents a weak chemical bond?

- a. hydrogen bond
- b. atomic bond
- c. covalent bond
- d. nonpolar covalent bond

Solution:

A

Free Response**Exercise:**

Problem: What makes ionic bonds different from covalent bonds?

Solution:

Ionic bonds are created between ions. The electrons are not shared between the atoms, but rather are associated more with one ion than the other. Ionic bonds are strong bonds, but are weaker than covalent bonds, meaning it takes less energy to break an ionic bond compared with a covalent one.

Exercise:

Problem:

Why are hydrogen bonds and van der Waals interactions necessary for cells?

Solution:

Hydrogen bonds and van der Waals interactions form weak associations between different molecules or within different regions of the same molecule. They provide the structure and shape necessary for proteins and DNA within cells so that they function properly.

Glossary

anion

negative ion that is formed by an atom gaining one or more electrons

atom

the smallest unit of matter that retains all of the chemical properties of an element

atomic mass

calculated mean of the mass number for an element's isotopes

atomic number

total number of protons in an atom

balanced chemical equation

statement of a chemical reaction with the number of each type of atom equalized for both the products and reactants

cation

positive ion that is formed by an atom losing one or more electrons

chemical bond

interaction between two or more of the same or different atoms that results in the formation of molecules

chemical reaction

process leading to the rearrangement of atoms in molecules

chemical reactivity

the ability to combine and to chemically bond with each other

compound

substance composed of molecules consisting of atoms of at least two different elements

covalent bond

type of strong bond formed between two of the same or different elements; forms when electrons are shared between atoms

electrolyte

ion necessary for nerve impulse conduction, muscle contractions and water balance

electron

negatively charged subatomic particle that resides outside of the nucleus in the electron orbital; lacks functional mass and has a negative charge of -1 unit

electron configuration

arrangement of electrons in an atom's electron shell (for example, $1s^2 2s^2 2p^6$)

electron orbital

how electrons are spatially distributed surrounding the nucleus; the area where an electron is most likely to be found

electron transfer

movement of electrons from one element to another; important in creation of ionic bonds

electronegativity

ability of some elements to attract electrons (often of hydrogen atoms), acquiring partial negative charges in molecules and creating partial positive charges on the hydrogen atoms

element

one of 118 unique substances that cannot be broken down into smaller substances; each element has unique properties and a specified number of protons

equilibrium

steady state of relative reactant and product concentration in reversible chemical reactions in a closed system

hydrogen bond

weak bond between slightly positively charged hydrogen atoms to slightly negatively charged atoms in other molecules

inert gas

(also, noble gas) element with filled outer electron shell that is unreactive with other atoms

ion

atom or chemical group that does not contain equal numbers of protons and electrons

ionic bond

chemical bond that forms between ions with opposite charges (cations and anions)

irreversible chemical reaction

chemical reaction where reactants proceed uni-directionally to form products

isotope

one or more forms of an element that have different numbers of neutrons

law of mass action

chemical law stating that the rate of a reaction is proportional to the concentration of the reacting substances

mass number

total number of protons and neutrons in an atom

matter

anything that has mass and occupies space

molecule

two or more atoms chemically bonded together

neutron

uncharged particle that resides in the nucleus of an atom; has a mass of one amu

noble gas

see inert gas

nonpolar covalent bond

type of covalent bond that forms between atoms when electrons are shared equally between them

nucleus

core of an atom; contains protons and neutrons

octet rule

rule that atoms are most stable when they hold eight electrons in their outermost shells

orbital

region surrounding the nucleus; contains electrons

periodic table

organizational chart of elements indicating the atomic number and atomic mass of each element; provides key information about the properties of the elements

polar covalent bond

type of covalent bond that forms as a result of unequal sharing of electrons, resulting in the creation of slightly positive and slightly negative charged regions of the molecule

product

molecule found on the right side of a chemical equation

proton

positively charged particle that resides in the nucleus of an atom; has a mass of one amu and a charge of +1

radioisotope

isotope that emits radiation composed of subatomic particles to form more stable elements

reactant

molecule found on the left side of a chemical equation

reversible chemical reaction

chemical reaction that functions bi-directionally, where products may turn into reactants if their concentration is great enough

valence shell

outermost shell of an atom

van der Waals interaction

very weak interaction between molecules due to temporary charges
attracting atoms that are very close together

Bis2A 02.2 Carbon v1.2

By the end of this section, you will be able to:

- Explain why carbon is important for life
- Describe the role of functional groups in biological molecules

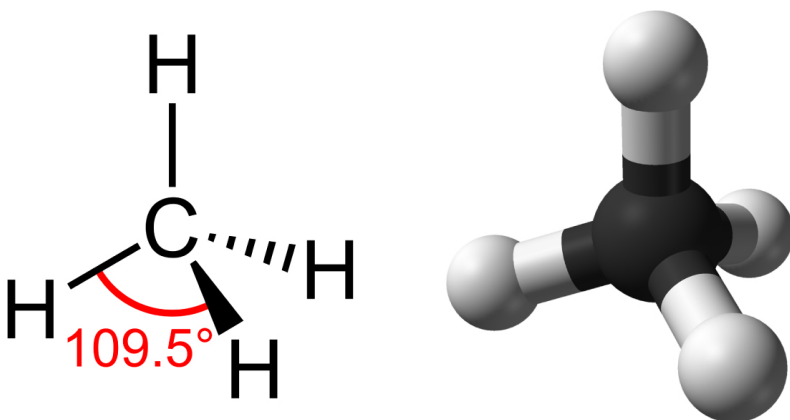
Cells are made of many complex molecules called macromolecules, such as proteins, nucleic acids (RNA and DNA), carbohydrates, and lipids. The macromolecules are a subset of **organic molecules** (any carbon-containing liquid, solid, or gas) that are especially important for life. The fundamental component for all of these macromolecules is carbon. The carbon atom has unique properties that allow it to form covalent bonds to as many as four different atoms, making this versatile element ideal to serve as the basic structural component, or “backbone,” of the macromolecules.

Individual carbon atoms have an incomplete outermost electron shell. With an atomic number of 6 (six electrons and six protons), the first two electrons fill the inner shell, leaving four in the second shell. Therefore, carbon atoms can form up to four covalent bonds with other atoms to satisfy the octet rule. The methane molecule provides an example: it has the chemical formula CH_4 . Each of its four hydrogen atoms forms a single covalent bond with the carbon atom by sharing a pair of electrons. This results in a filled outermost shell.

Hydrocarbons

Hydrocarbons are organic molecules consisting entirely of carbon and hydrogen, such as methane (CH_4) described above. We often use hydrocarbons in our daily lives as fuels—like the propane in a gas grill or the butane in a lighter. The many covalent bonds between the atoms in hydrocarbons store a great amount of energy, which is released when these molecules are burned (oxidized). Methane, an excellent fuel, is the simplest hydrocarbon molecule, with a central carbon atom bonded to four different hydrogen atoms, as illustrated in [\[link\]](#). The geometry of the methane molecule, where the atoms reside in three dimensions, is determined by the shape of its electron orbitals. The carbons and the four hydrogen atoms

form a shape known as a tetrahedron, with four triangular faces; for this reason, methane is described as having tetrahedral geometry.



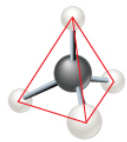
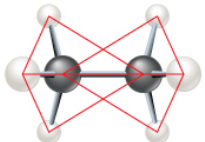
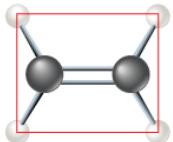
Methane has a tetrahedral geometry, with each of the four hydrogen atoms spaced 109.5° apart.

As the backbone of the large molecules of living things, hydrocarbons may exist as linear carbon chains, carbon rings, or combinations of both. Furthermore, individual carbon-to-carbon bonds may be single, double, or triple covalent bonds, and each type of bond affects the geometry of the molecule in a specific way. This three-dimensional shape or conformation of the large molecules of life (macromolecules) is critical to how they function.

Hydrocarbon Chains

Hydrocarbon chains are formed by successive bonds between carbon atoms and may be branched or unbranched. Furthermore, the overall geometry of the molecule is altered by the different geometries of single, double, and triple covalent bonds, illustrated in [\[link\]](#). The hydrocarbons ethane, ethene, and ethyne serve as examples of how different carbon-to-carbon bonds

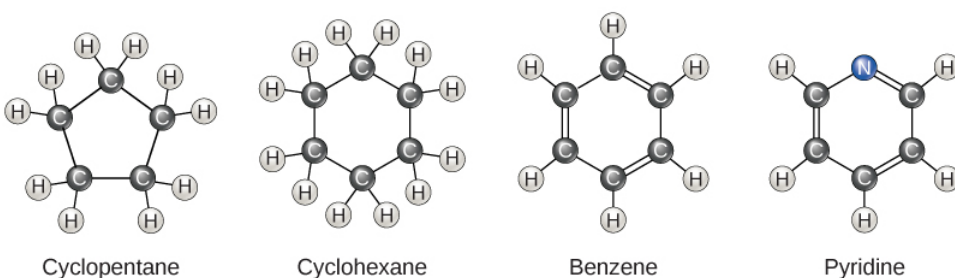
affect the geometry of the molecule. The names of all three molecules start with the prefix “eth-,” which is the prefix for two carbon hydrocarbons. The suffixes “-ane,” “-ene,” and “-yne” refer to the presence of single, double, or triple carbon-carbon bonds, respectively. Thus, propane, propene, and propyne follow the same pattern with three carbon molecules, butane, butene, and butyne for four carbon molecules, and so on. Double and triple bonds change the geometry of the molecule: single bonds allow rotation along the axis of the bond, whereas double bonds lead to a planar configuration and triple bonds to a linear one. These geometries have a significant impact on the shape a particular molecule can assume.

Methane (CH ₄)	Ethane (C ₂ H ₆)	Ethene (C ₂ H ₄)
		
Tetrahedral (single bond)	Tetrahedral (single bond)	Planar (double bond)

When carbon forms single bonds with other atoms, the shape is tetrahedral. When two carbon atoms form a double bond, the shape is planar, or flat. Single bonds, like those found in ethane, are able to rotate. Double bonds, like those found in ethene cannot rotate, so the atoms on either side are locked in place.

Hydrocarbon Rings

So far, the hydrocarbons we have discussed have been **aliphatic hydrocarbons**, which consist of linear chains of carbon atoms. Another type of hydrocarbon, **aromatic hydrocarbons**, consists of closed rings of carbon atoms. Ring structures are found in hydrocarbons, sometimes with the presence of double bonds, which can be seen by comparing the structure of cyclohexane to benzene in [\[link\]](#). Examples of biological molecules that incorporate the benzene ring include some amino acids and cholesterol and its derivatives, including the hormones estrogen and testosterone. The benzene ring is also found in the herbicide 2,4-D. Benzene is a natural component of crude oil and has been classified as a carcinogen. Some hydrocarbons have both aliphatic and aromatic portions; beta-carotene is an example of such a hydrocarbon.



Carbon can form five-and six membered rings. Single or double bonds may connect the carbons in the ring, and nitrogen may be substituted for carbon.

Exercise:

Converting chemical structures into chemical formulas

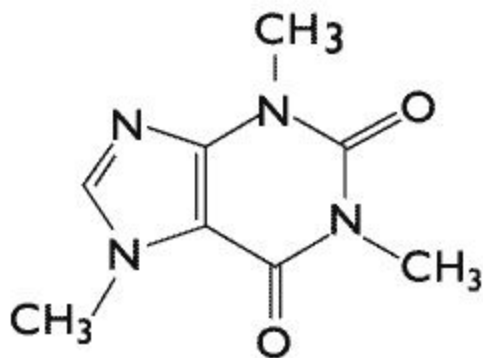
Problem:

Using figure 3 above. Which of the following correspond to Benzene?

- a. C₅H₁₀
- b. C₆H₁₂
- c. C₆H₆
- d. C₅H₅N

Solution:

C



The structure of caffeine

Exercise:

Converting chemical structures into chemical formulas

Problem:

Can you convert the chemical structure of caffeine shown in the picture above (figure 4) into a chemical formula?

- a. C₃H₁₀N₄O₂
- b. C₈H₁₀N₄O₂
- c. C₃H₉N₄O₂
- d. C₈H₉N₄O₂

Solution:

B

Isomers

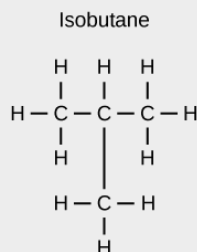
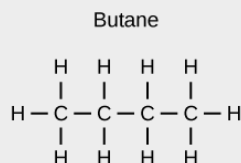
The three-dimensional placement of atoms and chemical bonds within organic molecules is central to understanding their chemistry. Molecules that share the same chemical formula but differ in the placement (structure) of their atoms and/or chemical bonds are known as **isomers**. **Structural isomers** (like butane and isobutene shown in [\[link\]](#)**a**) differ in the placement of their covalent bonds: both molecules have four carbons and ten hydrogens (C_4H_{10}), but the different arrangement of the atoms within the molecules leads to differences in their chemical properties. For example, due to their different chemical properties, butane is suited for use as a fuel for cigarette lighters and torches, whereas isobutene is suited for use as a refrigerant and a propellant in spray cans.

Geometric isomers, on the other hand, have similar placements of their covalent bonds but differ in how these bonds are made to the surrounding atoms, especially in carbon-to-carbon double bonds. In the simple molecule butene (C_4H_8), the two methyl groups (CH_3) can be on either side of the double covalent bond central to the molecule, as illustrated in [\[link\]](#)**b**. When the carbons are bound on the same side of the double bond, this is the *cis* configuration; if they are on opposite sides of the double bond, it is a *trans* configuration. In the *trans* configuration, the carbons form a more or less linear structure, whereas the carbons in the *cis* configuration make a bend (change in direction) of the carbon backbone.

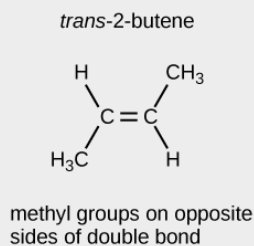
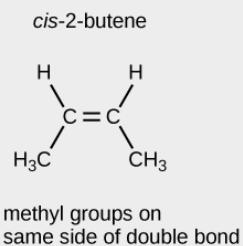
Note:

Art Connection

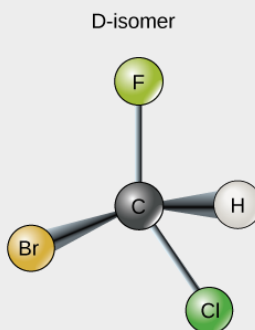
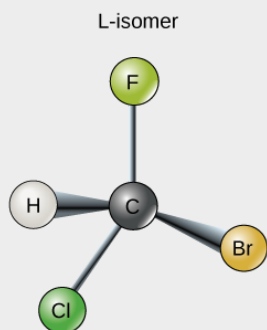
(a) Structural isomers



(b) Geometric isomers



(c) Enantiomers

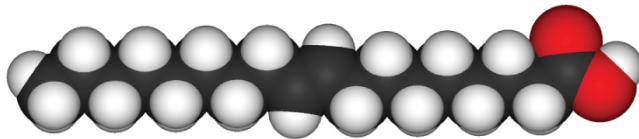


Molecules that have the same number and type of atoms arranged differently are called isomers. (a) Structural isomers have a different covalent arrangement of atoms. (b) Geometric isomers have a different arrangement of atoms around a double bond. (c) Enantiomers are mirror images of each other.

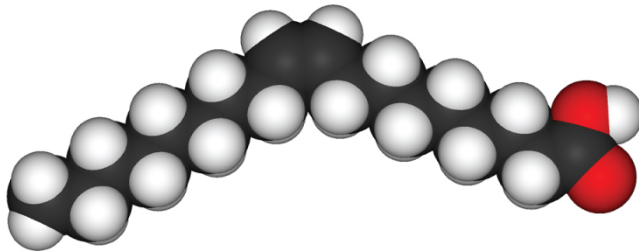
Which of the following statements is false?

- a. Molecules with the formulas $\text{CH}_3\text{CH}_2\text{COOH}$ and $\text{C}_3\text{H}_6\text{O}_2$ could be structural isomers.
- b. Molecules must have a double bond to be *cis-trans* isomers.
- c. To be enantiomers, a molecule must have at least three different atoms or groups connected to a central carbon.
- d. To be enantiomers, a molecule must have at least four different atoms or groups connected to a central carbon.

In triglycerides (fats and oils), long carbon chains known as fatty acids may contain double bonds, which can be in either the *cis* or *trans* configuration, illustrated in [\[link\]](#). Fats with at least one double bond between carbon atoms are unsaturated fats. When some of these bonds are in the *cis* configuration, the resulting bend in the carbon backbone of the chain means that triglyceride molecules cannot pack tightly, so they remain liquid (oil) at room temperature. On the other hand, triglycerides with *trans* double bonds (popularly called trans fats), have relatively linear fatty acids that are able to pack tightly together at room temperature and form solid fats. In the human diet, trans fats are linked to an increased risk of cardiovascular disease, so many food manufacturers have reduced or eliminated their use in recent years. In contrast to unsaturated fats, triglycerides without double bonds between carbon atoms are called saturated fats, meaning that they contain all the hydrogen atoms available. Saturated fats are a solid at room temperature and usually of animal origin.



Eliadic acid

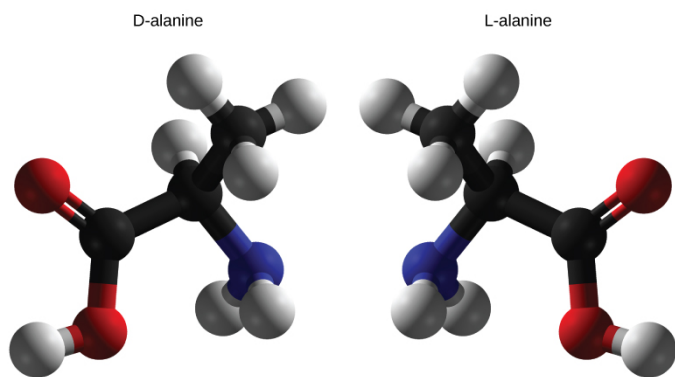


Oleic acid

These space-filling models show a *cis* (oleic acid) and a *trans* (eliadic acid) fatty acid. Notice the bend in the molecule cause by the *cis* configuration.

Enantiomers

Enantiomers are molecules that share the same chemical structure and chemical bonds but differ in the three-dimensional placement of atoms so that they are mirror images. As shown in [\[link\]](#), an amino acid alanine example, the two structures are non-superimposable. In nature, only the L-forms of amino acids are used to make proteins. Some D forms of amino acids are seen in the cell walls of bacteria, but never in their proteins. Similarly, the D-form of glucose is the main product of photosynthesis and the L-form of the molecule is rarely seen in nature.



D-alanine and L-alanine are examples of enantiomers or mirror images. Only the L-forms of amino acids are used to make proteins.

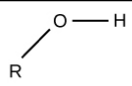

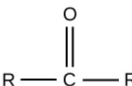
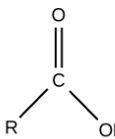
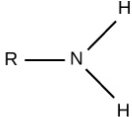
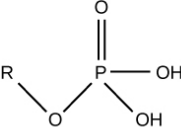
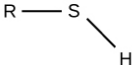
Functional Groups

Functional groups are groups of atoms that occur within molecules and confer specific chemical properties to those molecules. They are found along the “carbon backbone” of macromolecules. This carbon backbone is formed by chains and/or rings of carbon atoms with the occasional substitution of an element such as nitrogen or oxygen. Molecules with other elements in their carbon backbone are **substituted hydrocarbons**. For a short review of functional groups important in biology, visit the YouTube link by clicking [here](#), its a detailed video -at 13min - but more relevant to biology than other videos.

The functional groups in a macromolecule are usually attached to the carbon backbone at one or several different places along its chain and/or ring structure. Each of the four types of macromolecules—proteins, lipids, carbohydrates, and nucleic acids—has its own characteristic set of functional groups that contributes greatly to its differing chemical properties and its function in living organisms.

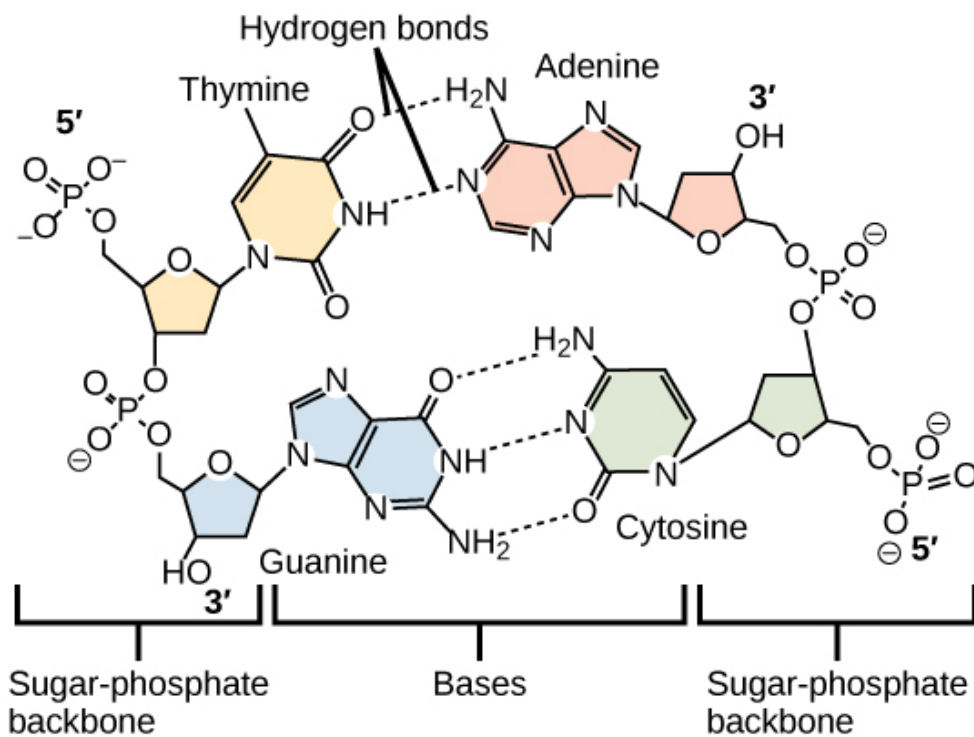
A functional group can participate in specific chemical reactions. Some of the important functional groups in biological molecules are shown in [\[link\]](#);

they include: hydroxyl, methyl, carbonyl, carboxyl, amino, phosphate, and sulfhydryl. These groups play an important role in the formation of molecules like DNA, proteins, carbohydrates, and lipids. Functional groups are usually classified as hydrophobic or hydrophilic depending on their charge or polarity characteristics. An example of a hydrophobic group is the non-polar methane molecule. Among the hydrophilic functional groups is the carboxyl group found in amino acids, some amino acid side chains, and the fatty acids that form triglycerides and phospholipids. This carboxyl group ionizes to release hydrogen ions (H^+) from the $COOH$ group resulting in the negatively charged COO^- group; this contributes to the hydrophilic nature of whatever molecule it is found on. Other functional groups, such as the carbonyl group, have a partially negatively charged oxygen atom that may form hydrogen bonds with water molecules, again making the molecule more hydrophilic.

Functional Group	Structure	Properties
Hydroxyl		Polar
Methyl		Nonpolar
Carbonyl		Polar
Carboxyl		Charged, ionizes to release H^+ . Since carboxyl groups can release H^+ ions into solution, they are considered acidic.
Amino		Charged, accepts H^+ to form NH_3^+ . Since amino groups can remove H^+ from solution, they are considered basic.
Phosphate		Charged, ionizes to release H^+ . Since phosphate groups can release H^+ ions into solution, they are considered acidic.
Sulfhydryl		Polar

The functional groups shown here are found in many different biological molecules.

Hydrogen bonds between functional groups (within the same molecule or between different molecules) are important to the function of many macromolecules and help them to fold properly into and maintain the appropriate shape for functioning. Hydrogen bonds are also involved in various recognition processes, such as DNA complementary base pairing and the binding of an enzyme to its substrate, as illustrated in [\[link\]](#).



Hydrogen bonds connect two strands of DNA together to create the double-helix structure.

Section Summary

The unique properties of carbon make it a central part of biological molecules. Carbon binds to oxygen, hydrogen, and nitrogen covalently to form the many molecules important for cellular function. Carbon has four electrons in its outermost shell and can form four bonds. Carbon and hydrogen can form hydrocarbon chains or rings. Functional groups are groups of atoms that confer specific properties to hydrocarbon (or substituted hydrocarbon) chains or rings that define their overall chemical characteristics and function.

Art Connections

Exercise:

Problem: [\[link\]](#) Which of the following statements is false?

- a. Molecules with the formulas $\text{CH}_3\text{CH}_2\text{COOH}$ and $\text{C}_3\text{H}_6\text{O}_2$ could be structural isomers.
- b. Molecules must have a double bond to be *cis-trans* isomers.
- c. To be enantiomers, a molecule must have at least three different atoms or groups connected to a central carbon.
- d. To be enantiomers, a molecule must have at least four different atoms or groups connected to a central carbon.

Solution:

[\[link\]](#) C

Review Questions

Exercise:

Problem:

Each carbon molecule can bond with as many as _____ other atom(s) or molecule(s).

- a. one
- b. two
- c. six
- d. four

Solution:

D

Exercise:**Problem:**

Which of the following is not a functional group that can bond with carbon?

- a. sodium
- b. hydroxyl
- c. phosphate
- d. carbonyl

Solution:

A

Free Response**Exercise:**

Problem: What property of carbon makes it essential for organic life?

Solution:

Carbon is unique and found in all living things because it can form up to four covalent bonds between atoms or molecules. These can be nonpolar or polar covalent bonds, and they allow for the formation of long chains of carbon molecules that combine to form proteins and DNA.

Exercise:**Problem:**

Compare and contrast saturated and unsaturated triglycerides.

Solution:

Saturated triglycerides contain no double bonds between carbon atoms; they are usually solid at room temperature. Unsaturated triglycerides contain at least one double bond between carbon atoms and are usually liquid at room temperature.

Glossary

aliphatic hydrocarbon

hydrocarbon consisting of a linear chain of carbon atoms

aromatic hydrocarbon

hydrocarbon consisting of closed rings of carbon atoms

enantiomers

molecules that share overall structure and bonding patterns, but differ in how the atoms are three dimensionally placed such that they are mirror images of each other

functional group

group of atoms that provides or imparts a specific function to a carbon skeleton

geometric isomer

isomer with similar bonding patterns differing in the placement of atoms alongside a double covalent bond

hydrocarbon

molecule that consists only of carbon and hydrogen

isomers

molecules that differ from one another even though they share the same chemical formula

organic molecule

any molecule containing carbon (except carbon dioxide)

structural isomers

molecules that share a chemical formula but differ in the placement of their chemical bonds

substituted hydrocarbon

hydrocarbon chain or ring containing an atom of another element in place of one of the backbone carbons

Bis2A 02.2 Appendix I Working with functional groups: Aldehydes, Ketones Carboxylic Acids and Esters

By the end of this section, you will be able to:

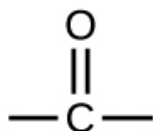
- Describe the structure and properties of aldehydes, ketones, carboxylic acids and esters

Functional Groups

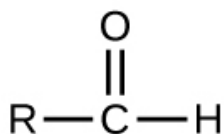
A functional group is a specific group of atoms within a molecule that is responsible for characteristic chemical reactions of that molecule. Many biologically active molecules contain one or more functional groups. For example the amino acid glycine has two functional groups, the carboxylic acid and the amino group. In this section we will review the major carbon containing functional groups found in biological molecules. These include: **Aldehydes**, **Ketones**, **Carboxylic acids**, and **Esters**. These classes of organic molecules contains a carbon atom connected to an oxygen atom by a double bond, commonly called a carbonyl group. The trigonal planar carbon in the carbonyl group can attach to two other substituents leading to several subfamilies (aldehydes, ketones, carboxylic acids and esters) described in this section.

Aldehydes and Ketones

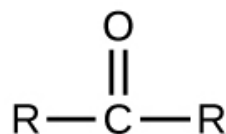
Both **aldehydes** and **ketones** contain a **carbonyl group**, a functional group with a carbon-oxygen double bond. The names for aldehyde and ketone compounds are derived using similar nomenclature rules as for alkanes and alcohols, and include the class-identifying suffixes *-al* and *-one*, respectively:



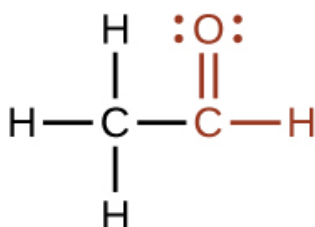
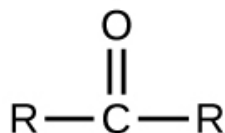
In an aldehyde, the carbonyl group is bonded to at least one hydrogen atom. In a ketone, the carbonyl group is bonded to two carbon atoms:



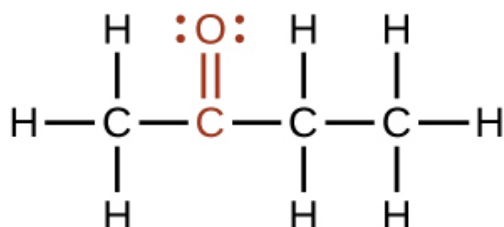
Functional group
of an aldehyde



Functional group
of a ketone



CH3CHO
An aldehyde
ethanal (acetaldehyde)

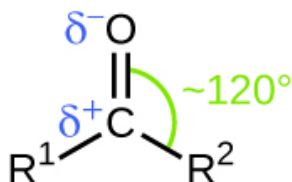


CH3COCH2CH3
A ketone
butanone

As text, an aldehyde group is represented as -CHO; a ketone is represented as -C(O)- or -CO-.

In both aldehydes and ketones, the geometry around the carbon atom in the carbonyl group is trigonal planar; the carbon atom exhibits sp^2 hybridization. Two of the sp^2 orbitals on the carbon atom in the carbonyl group are used to form σ bonds to the other carbon or hydrogen atoms in a molecule. The remaining sp^2 hybrid orbital forms a σ bond to the oxygen atom. The unhybridized p orbital on the carbon atom in the carbonyl group overlaps a p orbital on the oxygen atom to form the π bond in the double bond.

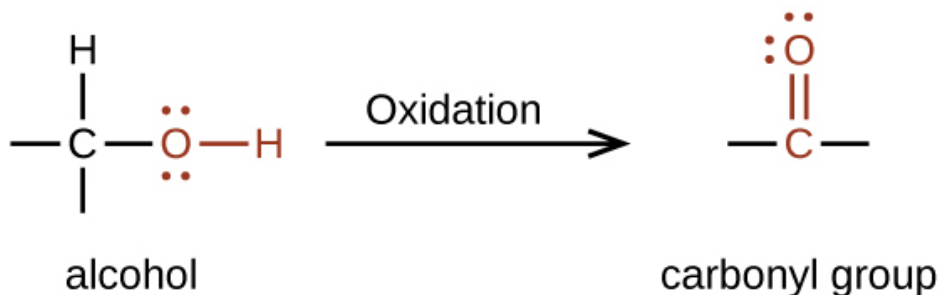
Like the $\text{C} = \text{O}$ bond in carbon dioxide, the $\text{C} = \text{O}$ bond of a carbonyl group is polar (recall that oxygen is significantly more electronegative than carbon, and the shared electrons are pulled toward the oxygen atom and away from the carbon atom). Many of the reactions of aldehydes and ketones start with the reaction between a Lewis base and the carbon atom at the positive end of the polar $\text{C} = \text{O}$ bond to yield an unstable intermediate that subsequently undergoes one or more structural rearrangements to form the final product ([link](#)).



The carbonyl group is polar, and the geometry of the bonds around

the central carbon is trigonal planar.

The importance of molecular structure in the reactivity of organic compounds is illustrated by the reactions that produce aldehydes and ketones. We can prepare a carbonyl group by oxidation of an alcohol—for organic molecules, oxidation of a carbon atom is said to occur when a carbon-hydrogen bond is replaced by a carbon-oxygen bond. The reverse reaction—replacing a carbon-oxygen bond by a carbon-hydrogen bond—is a reduction of that carbon atom. Recall that oxygen is generally assigned a -2 oxidation number unless it is elemental or attached to a fluorine. Hydrogen is generally assigned an oxidation number of $+1$ unless it is attached to a metal. Since carbon does not have a specific rule, its oxidation number is determined algebraically by factoring the atoms it is attached to and the overall charge of the molecule or ion. In general, a carbon atom attached to an oxygen atom will have a more positive oxidation number and a carbon atom attached to a hydrogen atom will have a more negative oxidation number. This should fit nicely with your understanding of the polarity of C–O and C–H bonds. The other reagents and possible products of these reactions are beyond the scope of this chapter, so we will focus only on the changes to the carbon atoms:



Example:

Oxidation and Reduction in Organic Chemistry

Methane represents the completely reduced form of an organic molecule that contains one carbon atom. Sequentially replacing each of the carbon-hydrogen bonds with a carbon-oxygen bond would lead to an alcohol, then an aldehyde, then a carboxylic acid (discussed later), and, finally, carbon dioxide:

Equation:



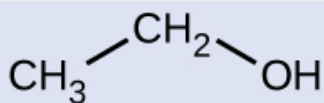
What are the oxidation numbers for the carbon atoms in the molecules shown here?

Solution

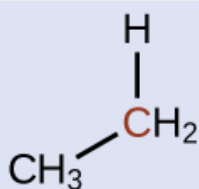
In this example, we can calculate the oxidation number (review the chapter on oxidation-reduction reactions if necessary) for the carbon atom in each case (note how this would become difficult for larger molecules with additional carbon atoms and hydrogen atoms, which is why organic chemists use the definition dealing with replacing C–H bonds with C–O bonds described). For CH_4 , the carbon atom carries a -4 oxidation number (the hydrogen atoms are assigned oxidation numbers of $+1$ and the carbon atom balances that by having an oxidation number of -4). For the alcohol (in this case, methanol), the carbon atom has an oxidation number of -2 (the oxygen atom is assigned -2 , the four hydrogen atoms each are assigned $+1$, and the carbon atom balances the sum by having an oxidation number of -2 ; note that compared to the carbon atom in CH_4 , this carbon atom has lost two electrons so it was oxidized); for the aldehyde, the carbon atom's oxidation number is 0 (-2 for the oxygen atom and $+1$ for each hydrogen atom already balances to 0 , so the oxidation number for the carbon atom is 0); for the carboxylic acid, the carbon atom's oxidation number is $+2$ (two oxygen atoms each at -2 and two hydrogen atoms at $+1$); and for carbon dioxide, the carbon atom's oxidation number is $+4$ (here, the carbon atom needs to balance the -4 sum from the two oxygen atoms).

Check Your Learning

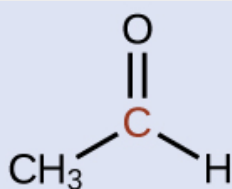
Indicate whether the marked carbon atoms in the three molecules here are oxidized or reduced relative to the marked carbon atom in ethanol:



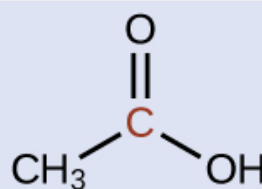
There is no need to calculate oxidation states in this case; instead, just compare the types of atoms bonded to the marked carbon atoms:



(a)



(b)



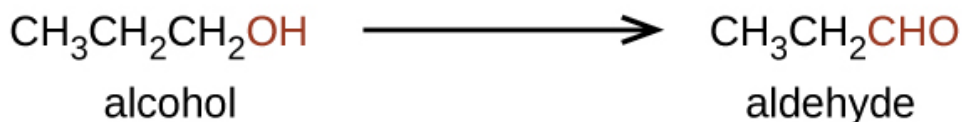
(c)

Note:

Answer:

(a) reduced (bond to oxygen atom replaced by bond to hydrogen atom); (b) oxidized (one bond to hydrogen atom replaced by one bond to oxygen atom); (c) oxidized (2 bonds to hydrogen atoms have been replaced by bonds to an oxygen atom)

Aldehydes are commonly prepared by the oxidation of alcohols whose –OH functional group is located on the carbon atom at the end of the chain of carbon atoms in the alcohol:



Alcohols that have their –OH groups in the middle of the chain are necessary to synthesize a ketone, which requires the carbonyl group to be bonded to two other carbon atoms:



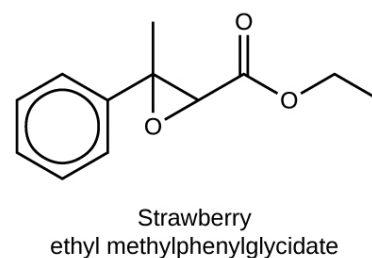
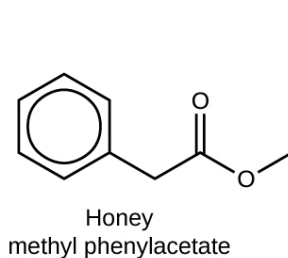
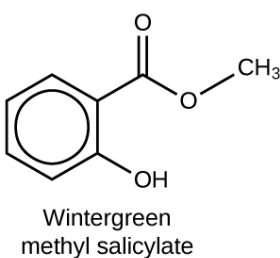
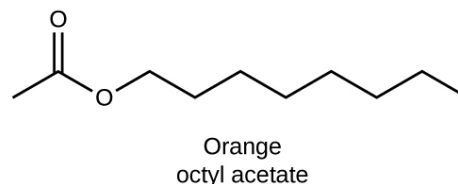
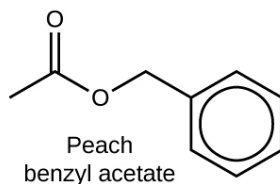
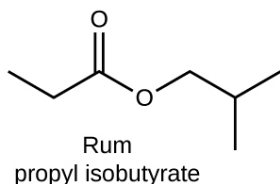
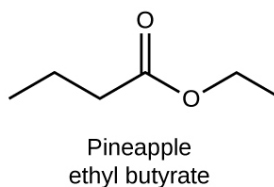
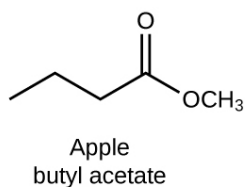
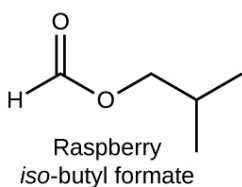
An alcohol with its –OH group bonded to a carbon atom that is bonded to no or one other carbon atom will form an aldehyde. An alcohol with its –OH group attached to two other carbon atoms will form a ketone. If three carbons are attached to the carbon bonded to the –OH, the molecule will not have a C–H bond to be replaced, so it will not be susceptible to oxidation.

Formaldehyde, an aldehyde with the formula HCHO, is a colorless gas with a pungent and irritating odor. It is sold in an aqueous solution called formalin, which contains about 37% formaldehyde by weight. Formaldehyde causes coagulation of proteins, so it kills bacteria (and any other living organism) and stops many of the biological processes that cause tissue to decay. Thus, formaldehyde is used for preserving tissue specimens and embalming bodies. It is also used to sterilize soil or other materials. Formaldehyde is used in the manufacture of Bakelite, a hard plastic having high chemical and electrical resistance.

Dimethyl ketone, CH₃COCH₃, commonly called acetone, is the simplest ketone. It is made commercially by fermenting corn or molasses, or by oxidation of 2-propanol. Acetone is a colorless liquid. Among its many uses are as a solvent for lacquer (including fingernail polish), cellulose acetate, cellulose nitrate, acetylene, plastics, and varnishes; as a paint and varnish remover; and as a solvent in the manufacture of pharmaceuticals and chemicals.

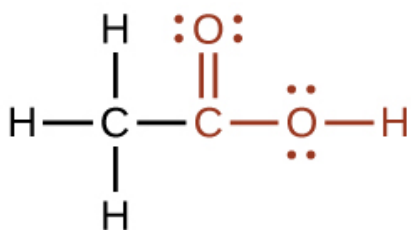
Carboxylic Acids and Esters

The odor of vinegar is caused by the presence of acetic acid, a carboxylic acid, in the vinegar. The odor of ripe bananas and many other fruits is due to the presence of esters, compounds that can be prepared by the reaction of a carboxylic acid with an alcohol. Because esters do not have hydrogen bonds between molecules, they have lower vapor pressures than the alcohols and carboxylic acids from which they are derived (see [\[link\]](#)).

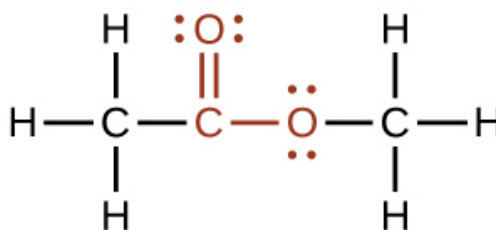


Esters are responsible for the odors associated with various plants and their fruits.

Both **carboxylic acids** and **esters** contain a carbonyl group with a second oxygen atom bonded to the carbon atom in the carbonyl group by a single bond. In a carboxylic acid, the second oxygen atom also bonds to a hydrogen atom. In an ester, the second oxygen atom bonds to another carbon atom. The names for carboxylic acids and esters include prefixes that denote the lengths of the carbon chains in the molecules and are derived following nomenclature rules similar to those for inorganic acids and salts (see these examples):



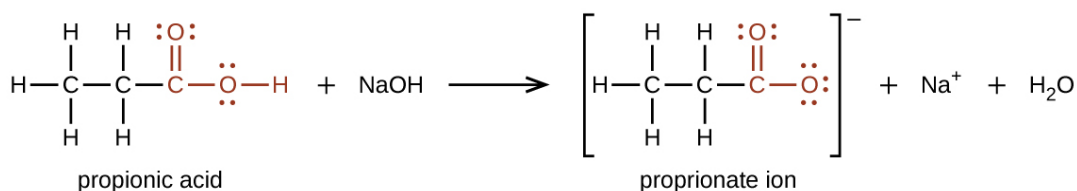
ethanoic acid
(acetic acid)



methyl ethanoate
(methyl acetate)

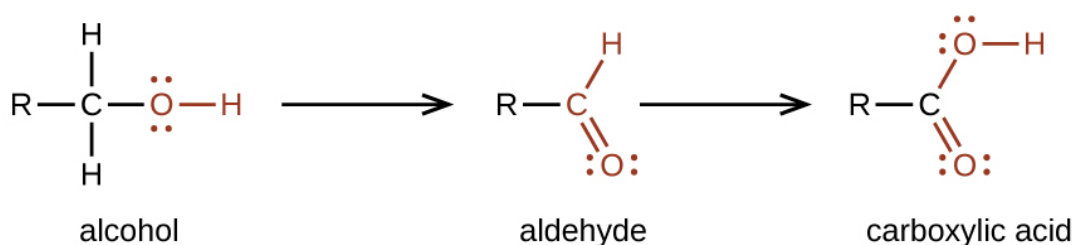
The functional groups for an acid and for an ester are shown in red in these formulas.

The hydrogen atom in the functional group of a carboxylic acid will react with a base to form an ionic salt:

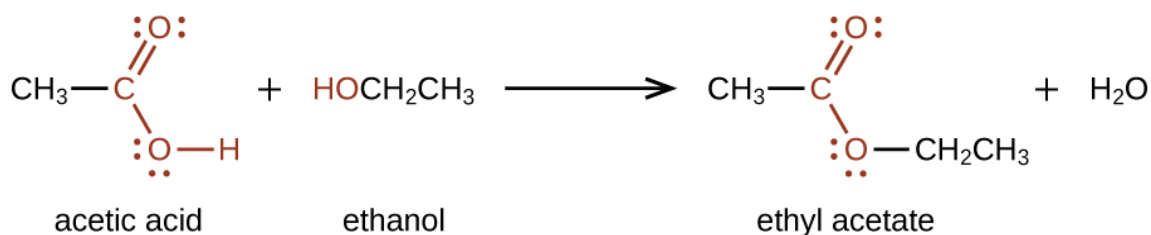


Carboxylic acids are weak acids (see the chapter on acids and bases), meaning they are not 100% ionized in water. Generally only about 1% of the molecules of a carboxylic acid dissolved in water are ionized at any given time. The remaining molecules are undissociated in solution.

We prepare carboxylic acids by the oxidation of aldehydes or alcohols whose $-\text{OH}$ functional group is located on the carbon atom at the end of the chain of carbon atoms in the alcohol:



Esters are produced by the reaction of acids with alcohols. For example, the ester ethyl acetate, $\text{CH}_3\text{CO}_2\text{CH}_2\text{CH}_3$, is formed when acetic acid reacts with ethanol:



The simplest carboxylic acid is formic acid, HCO_2H , known since 1670. Its name comes from the Latin word *formicus*, which means “ant”; it was first isolated by the distillation of red ants. It is partially responsible for the pain and irritation of ant and wasp stings, and is responsible for a characteristic odor of ants that can be sometimes detected in their nests.

Acetic acid, $\text{CH}_3\text{CO}_2\text{H}$, constitutes 3–6% vinegar. Cider vinegar is produced by allowing apple juice to ferment without oxygen present. Yeast cells present in the juice carry out the fermentation reactions. The fermentation reactions change the sugar present in the juice to ethanol, then to acetic acid. Pure acetic acid has a penetrating odor and produces painful

burns. It is an excellent solvent for many organic and some inorganic compounds, and it is essential in the production of cellulose acetate, a component of many synthetic fibers such as rayon.

The distinctive and attractive odors and flavors of many flowers, perfumes, and ripe fruits are due to the presence of one or more esters ([link](#)). Among the most important of the natural esters are fats (such as lard, tallow, and butter) and oils (such as linseed, cottonseed, and olive oils), which are esters of the trihydroxyl alcohol glycerine, $\text{C}_3\text{H}_5(\text{OH})_3$, with large carboxylic acids, such as palmitic acid, $\text{CH}_3(\text{CH}_2)_{14}\text{CO}_2\text{H}$, stearic acid, $\text{CH}_3(\text{CH}_2)_{16}\text{CO}_2\text{H}$, and oleic acid, $\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{CO}_2\text{H}$. Oleic acid is an unsaturated acid; it contains a $\text{C}=\text{C}$ double bond. Palmitic and stearic acids are saturated acids that contain no double or triple bonds.



Over 350 different volatile molecules (many members of the ester family) have been identified in strawberries. (credit: Rebecca Siegel)

Key Concepts and Summary

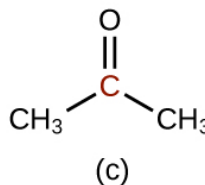
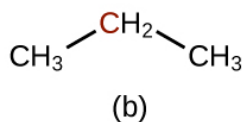
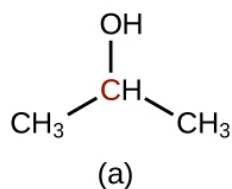
Functional groups related to the carbonyl group include the -CHO group of an aldehyde, the -CO- group of a ketone, the $\text{-CO}_2\text{H}$ group of a carboxylic acid, and the $\text{-CO}_2\text{R}$ group of an ester. The carbonyl group, a carbon-oxygen double bond, is the key structure in these classes of organic molecules: Aldehydes contain at least one hydrogen atom attached to the carbonyl carbon atom, ketones contain two carbon groups attached to the carbonyl carbon atom, carboxylic acids contain a hydroxyl group attached to the carbonyl carbon atom, and esters contain an oxygen atom attached to another carbon group connected to the carbonyl carbon atom. All of these compounds contain oxidized carbon atoms relative to the carbon atom of an alcohol group.

Chemistry End of Chapter Exercises

Exercise:

Problem:

Order the following molecules from least to most oxidized, based on the marked carbon atom:

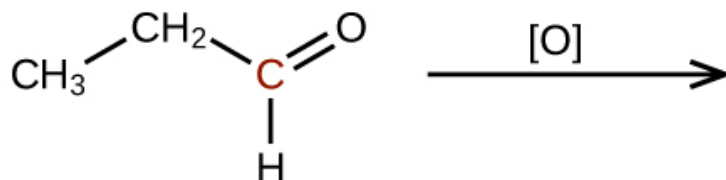


Exercise:

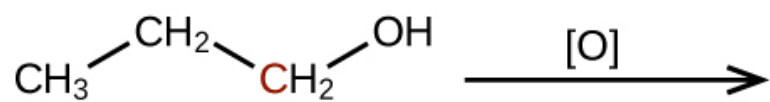
Problem:

Predict the products of oxidizing the molecules shown in this problem. In each case, identify the product that will result from the minimal increase in oxidation state for the highlighted carbon atom:

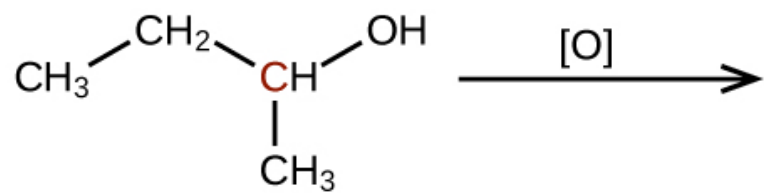
(a)



(b)

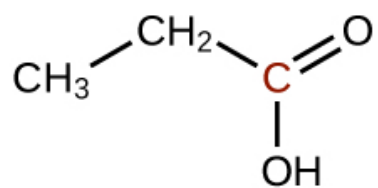


(c)



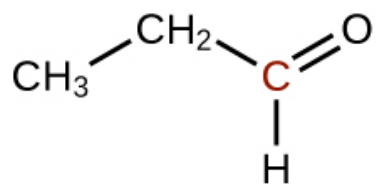
Solution:

(a)



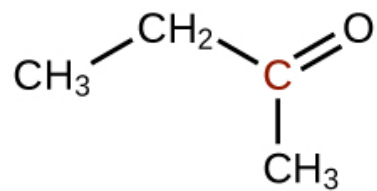
;

(b)



;

(c)

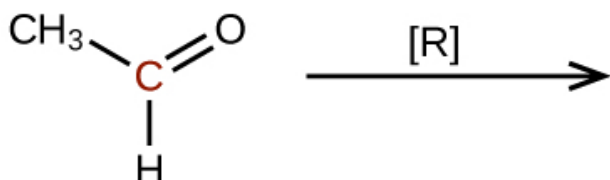


Exercise:

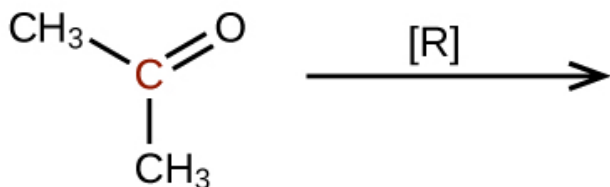
Problem:

Predict the products of reducing the following molecules. In each case, identify the product that will result from the minimal decrease in oxidation state for the highlighted carbon atom:

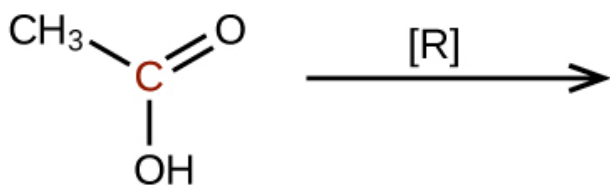
(a)



(b)



(c)

**Exercise:****Problem:**

Explain why it is not possible to prepare a ketone that contains only two carbon atoms.

Solution:

A ketone contains a group bonded to two additional carbon atoms; thus, a minimum of three carbon atoms are needed.

Exercise:

Problem:

How does hybridization of the substituted carbon atom change when an alcohol is converted into an aldehyde? An aldehyde to a carboxylic acid?

Exercise:**Problem:**

Fatty acids are carboxylic acids that have long hydrocarbon chains attached to a carboxylate group. How does a saturated fatty acid differ from an unsaturated fatty acid? How are they similar?

Solution:

Since they are both carboxylic acids, they each contain the -COOH functional group and its characteristics. The difference is the hydrocarbon chain in a saturated fatty acid contains no double or triple bonds, whereas the hydrocarbon chain in an unsaturated fatty acid contains one or more multiple bonds.

Exercise:**Problem:**

Write a condensed structural formula, such as CH_3CH_3 , and describe the molecular geometry at each carbon atom.

- (a) propene
- (b) 1-butanol
- (c) ethyl propyl ether
- (d) *cis*-4-bromo-2-heptene
- (e) 2,2,3-trimethylhexane
- (f) formaldehyde

Exercise:**Problem:**

Write a condensed structural formula, such as CH_3CH_3 , and describe the molecular geometry at each carbon atom.

- (a) 2-propanol
- (b) acetone

(c) dimethyl ether

(d) acetic acid

(e) 3-methyl-1-hexene

Solution:

(a) $\text{CH}_3\text{CH}(\text{OH})\text{CH}_3$: all carbons are tetrahedral; (b) $\text{CH}_3\text{C}(=\text{O})\text{CH}_3$: the end carbons are tetrahedral and the central carbon is trigonal planar; (c) CH_3OCH_3 : all are tetrahedral; (d) CH_3COOH : the methyl carbon is tetrahedral and the acid carbon is trigonal planar; (e) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_3)\text{CHCH}_2$: all are tetrahedral except the right-most two carbons, which are trigonal planar

Exercise:

Problem:

The foul odor of rancid butter is caused by butyric acid, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{H}$.

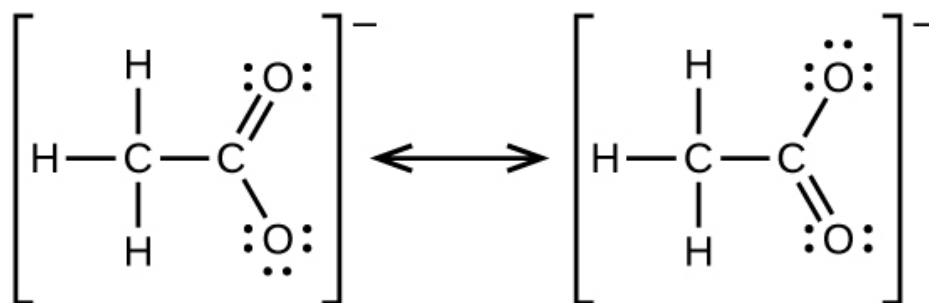
(a) Draw the Lewis structure and determine the oxidation number and hybridization for each carbon atom in the molecule.

(b) The esters formed from butyric acid are pleasant-smelling compounds found in fruits and used in perfumes. Draw the Lewis structure for the ester formed from the reaction of butyric acid with 2-propanol.

Exercise:

Problem: Write the two-resonance structures for the acetate ion.

Solution:



Exercise:

Problem:

Write two complete, balanced equations for each of the following reactions, one using condensed formulas and one using Lewis structures:

(a) ethanol reacts with propionic acid

(b) benzoic acid, $\text{C}_6\text{H}_5\text{CO}_2\text{H}$, is added to a solution of sodium hydroxide

Exercise:**Problem:**

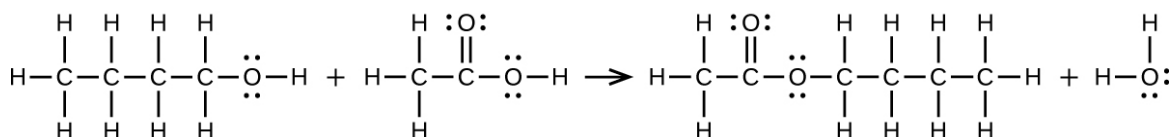
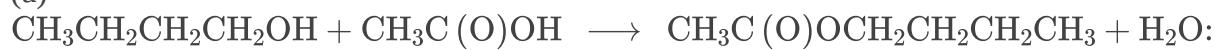
Write two complete balanced equations for each of the following reactions, one using condensed formulas and one using Lewis structures.

(a) 1-butanol reacts with acetic acid

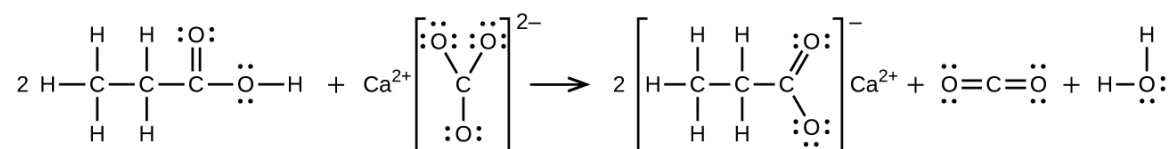
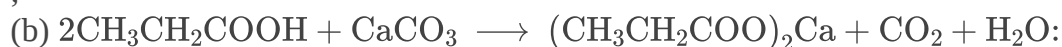
(b) propionic acid is poured onto solid calcium carbonate

Solution:

(a)



;

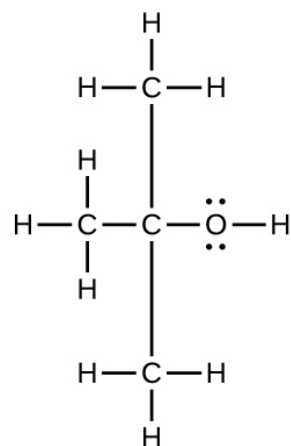
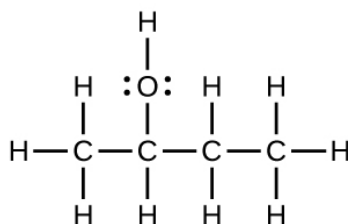
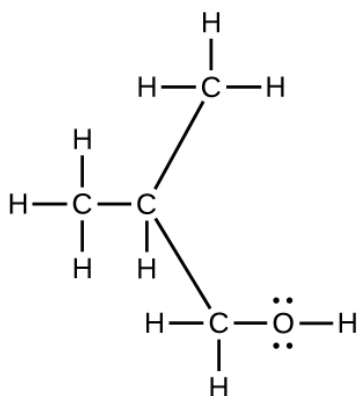
**Exercise:****Problem:**

Yields in organic reactions are sometimes low. What is the percent yield of a process that produces 13.0 g of ethyl acetate from 10.0 g of $\text{CH}_3\text{CO}_2\text{H}$?

Exercise:

Problem:

Alcohols A, B, and C all have the composition $C_4H_{10}O$. Molecules of alcohol A contain a branched carbon chain and can be oxidized to an aldehyde; molecules of alcohol B contain a linear carbon chain and can be oxidized to a ketone; and molecules of alcohol C can be oxidized to neither an aldehyde nor a ketone. Write the Lewis structures of these molecules.

Solution:**Glossary****aldehyde**

organic compound containing a carbonyl group bonded to two hydrogen atoms or a hydrogen atom and a carbon substituent

carbonyl group

carbon atom double bonded to an oxygen atom

carboxylic acid

organic compound containing a carbonyl group with an attached hydroxyl group

ester

organic compound containing a carbonyl group with an attached oxygen atom that is bonded to a carbon substituent

ketone

organic compound containing a carbonyl group with two carbon substituents attached to it

Bis2A 02.3 Water

By the end of this section, you will be able to:

- Describe the properties of water that are critical to maintaining life
- Explain why water is an excellent solvent
- Provide examples of water's cohesive and adhesive properties
- Discuss the role of acids, bases, and buffers in homeostasis

WATER

Why do scientists spend time looking for water on other planets? Why is water so important? It is because water is essential to life as we know it. Water is one of the more abundant molecules and the one most critical to life on Earth. Approximately 60–70 percent of the human body is made up of water. Without it, life as we know it simply would not exist.

The polarity of the water molecule and its resulting hydrogen bonding make water a unique substance with special properties that are intimately tied to the processes of life. Life originally evolved in a watery environment, and most of an organism's cellular chemistry and metabolism occur inside the watery contents of the cell's cytoplasm. Special properties of water are its high heat capacity and heat of vaporization, its ability to dissolve polar molecules, its cohesive and adhesive properties, and its dissociation into ions that leads to the generation of pH. Understanding these characteristics of water helps to elucidate its importance in maintaining life.

Water's Polarity

One of water's important properties is that it is composed of polar molecules: the hydrogen and oxygen within water molecules (H_2O) form polar covalent bonds. While there is no net charge to a water molecule, the polarity of water creates a slightly positive charge on hydrogen and a slightly negative charge on oxygen, contributing to water's properties of attraction. Water's charges are generated because oxygen is more electronegative than hydrogen, making it more likely that a shared electron would be found near the oxygen nucleus than the hydrogen nucleus, thus generating the partial negative charge near the oxygen.

As a result of water's polarity, each water molecule attracts other water molecules because of the opposite charges between water molecules, forming hydrogen bonds. Water also attracts or is attracted to other polar molecules and ions. A polar substance that interacts readily with or dissolves in water is referred to as **hydrophilic** (hydro- = “water”; -philic = “loving”). In contrast, non-polar molecules such as oils and fats do not interact well with water, as shown in [\[link\]](#) and separate from it rather than dissolve in it, as we see in salad dressings containing oil and vinegar (an acidic water solution). These nonpolar compounds are called **hydrophobic** (hydro- = “water”; -phobic = “fearing”).



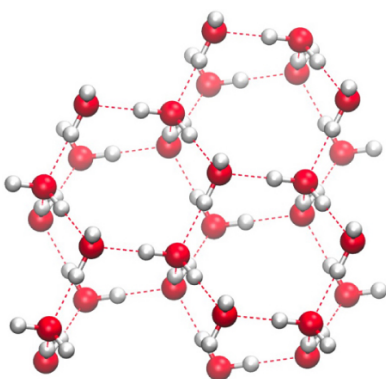
Oil and water do not mix. As this macro image of oil and water shows, oil does not dissolve in water but forms droplets instead. This is due to it being a nonpolar compound. (credit: Gautam Dogra).

Water's States: Gas, Liquid, and Solid

The formation of hydrogen bonds is an important quality of the liquid water that is crucial to life as we know it. As water molecules make hydrogen bonds with each other, water takes on some unique chemical characteristics compared to other liquids and, since living things have a high water content, understanding these chemical features is key to understanding life. In liquid water, hydrogen bonds are constantly formed and broken as the water molecules slide past each other. The breaking of these bonds is caused by the motion (kinetic energy) of the water molecules due to the heat contained in the system. When the heat is raised as water is boiled, the higher kinetic energy of the water molecules causes the hydrogen bonds to break completely and allows water molecules to escape into the air as gas (steam or water vapor). On the other hand, when the temperature of water is reduced and water freezes, the water molecules form a crystalline structure maintained by hydrogen bonding (there is not enough energy to break the hydrogen bonds) that makes ice less dense than liquid water, a phenomenon not seen in the solidification of other liquids.

Water's lower density in its solid form is due to the way hydrogen bonds are oriented as it freezes: the water molecules are pushed farther apart compared to liquid water. With most other liquids, solidification when the temperature drops includes the lowering of kinetic energy between molecules, allowing them to pack even more tightly than in liquid form and giving the solid a greater density than the liquid.

The lower density of ice, illustrated and pictured in [\[link\]](#), an anomaly, causes it to float at the surface of liquid water, such as in an iceberg or in the ice cubes in a glass of ice water. In lakes and ponds, ice will form on the surface of the water creating an insulating barrier that protects the animals and plant life in the pond from freezing. Without this layer of insulating ice, plants and animals living in the pond would freeze in the solid block of ice and could not survive. The detrimental effect of freezing on living organisms is caused by the expansion of ice relative to liquid water. The ice crystals that form upon freezing rupture the delicate membranes essential for the function of living cells, irreversibly damaging them. Cells can only survive freezing if the water in them is temporarily replaced by another liquid like glycerol.



(a)



(b)

Hydrogen bonding makes ice less dense than liquid water. The (a) lattice structure of ice makes it less dense than the freely flowing molecules of liquid water, enabling it to (b) float on water. (credit a: modification of work by Jane Whitney, image created using Visual Molecular Dynamics (VMD) software^[footnote]; credit b: modification of work by Carlos Ponte)

W. Humphrey W., A. Dalke, and K. Schulten, “VMD —Visual Molecular Dynamics,” *Journal of Molecular Graphics* 14 (1996): 33-38.

Note:

Link to Learning



Click [here](#) to see a 3-D animation of the structure of an ice lattice. (Image credit: Jane Whitney. Image created using Visual Molecular Dynamics

VMD software.^[footnote])

W. Humphrey W., A. Dalke, and K. Schulten, “VMD—Visual Molecular Dynamics,” *Journal of Molecular Graphics* 14 (1996): 33-38.

Water’s High Heat Capacity

Water’s high heat capacity is a property caused by hydrogen bonding among water molecules. Water has the highest **specific heat capacity** of any liquids. Specific heat is defined as the amount of heat one gram of a substance must absorb or lose to change its temperature by one degree Celsius. For water, this amount is one **calorie**. It therefore takes water a long time to heat and long time to cool. In fact, the specific heat capacity of water is about five times more than that of sand. This explains why the land cools faster than the sea. Due to its high heat capacity, water is used by warm blooded animals to more evenly disperse heat in their bodies: it acts in a similar manner to a car’s cooling system, transporting heat from warm places to cool places, causing the body to maintain a more even temperature.

Water’s Heat of Vaporization

Water also has a high **heat of vaporization**, the amount of energy required to change one gram of a liquid substance to a gas. A considerable amount of heat energy (586 cal) is required to accomplish this change in water. This process occurs on the surface of water. As liquid water heats up, hydrogen bonding makes it difficult to separate the liquid water molecules from each other, which is required for it to enter its gaseous phase (steam). As a result, water acts as a heat sink or heat reservoir and requires much more heat to boil than does a liquid such as ethanol (grain alcohol), whose hydrogen bonding with other ethanol molecules is weaker than water’s hydrogen bonding. Eventually, as water reaches its boiling point of 100° Celsius (212° Fahrenheit), the heat is able to break the hydrogen bonds between the water molecules, and the kinetic energy (motion) between the water molecules allows them to escape from the liquid as a gas. Even when below its boiling point, water’s individual molecules acquire enough energy from

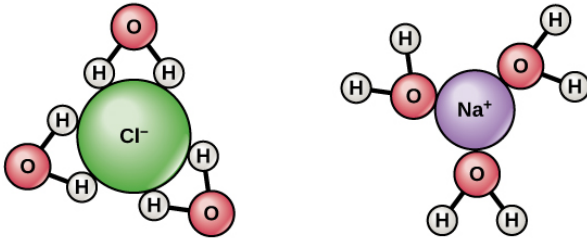
other water molecules such that some surface water molecules can escape and vaporize: this process is known as **evaporation**.

The fact that hydrogen bonds need to be broken for water to evaporate means that a substantial amount of energy is used in the process. As the water evaporates, energy is taken up by the process, cooling the environment where the evaporation is taking place. In many living organisms, including in humans, the evaporation of sweat, which is 90 percent water, allows the organism to cool so that homeostasis of body temperature can be maintained.

Water's Solvent Properties

Since water is a polar molecule with slightly positive and slightly negative charges, ions and polar molecules can readily dissolve in it. Therefore, water is referred to as a **solvent**, a substance capable of dissolving other polar molecules and ionic compounds. The charges associated with these molecules will form hydrogen bonds with water, surrounding the particle with water molecules. This is referred to as a **sphere of hydration**, or a hydration shell, as illustrated in [\[link\]](#) and serves to keep the particles separated or dispersed in the water.

When ionic compounds are added to water, the individual ions react with the polar regions of the water molecules and their ionic bonds are disrupted in the process of **dissociation**. Dissociation occurs when atoms or groups of atoms break off from molecules and form ions. Consider table salt (NaCl, or sodium chloride): when NaCl crystals are added to water, the molecules of NaCl dissociate into Na^+ and Cl^- ions, and spheres of hydration form around the ions, illustrated in [\[link\]](#). The positively charged sodium ion is surrounded by the partially negative charge of the water molecule's oxygen. The negatively charged chloride ion is surrounded by the partially positive charge of the hydrogen on the water molecule.



When table salt (NaCl) is mixed in water, spheres of hydration are formed around the ions.

Water's Cohesive and Adhesive Properties

Have you ever filled a glass of water to the very top and then slowly added a few more drops? Before it overflows, the water forms a dome-like shape above the rim of the glass. This water can stay above the glass because of the property of **cohesion**. In cohesion, water molecules are attracted to each other (because of hydrogen bonding), keeping the molecules together at the liquid-gas (water-air) interface, although there is no more room in the glass.

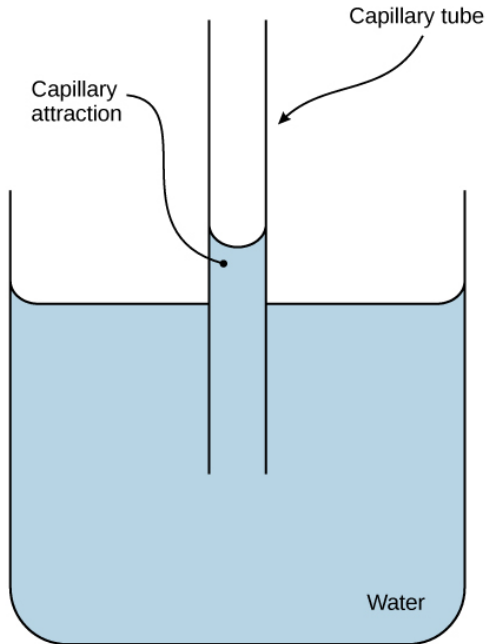
Cohesion allows for the development of **surface tension**, the capacity of a substance to withstand being ruptured when placed under tension or stress. This is also why water forms droplets when placed on a dry surface rather than being flattened out by gravity. When a small scrap of paper is placed onto the droplet of water, the paper floats on top of the water droplet even though paper is denser (heavier) than the water. Cohesion and surface tension keep the hydrogen bonds of water molecules intact and support the item floating on the top. It's even possible to "float" a needle on top of a glass of water if it is placed gently without breaking the surface tension, as shown in [\[link\]](#).



The weight of the needle is pulling the surface downward; at the same time, the surface tension is pulling it up, suspending it on the surface of the water and keeping it from sinking. Notice the indentation in the water around the needle.

(credit: Cory Zanker)

These cohesive forces are related to water's property of **adhesion**, or the attraction between water molecules and other molecules. This attraction is sometimes stronger than water's cohesive forces, especially when the water is exposed to charged surfaces such as those found on the inside of thin glass tubes known as capillary tubes. Adhesion is observed when water "climbs" up the tube placed in a glass of water: notice that the water appears to be higher on the sides of the tube than in the middle. This is because the water molecules are attracted to the charged glass walls of the capillary more than they are to each other and therefore adhere to it. This type of adhesion is called **capillary action**, and is illustrated in [\[link\]](#).



Capillary action in a glass tube is caused by the adhesive forces exerted by the internal surface of the glass exceeding the cohesive forces between the water molecules themselves. (credit: modification of work by Pearson-Scott Foresman, donated to the Wikimedia Foundation)

Why are cohesive and adhesive forces important for life? Cohesive and adhesive forces are important for the transport of water from the roots to the leaves in plants. These forces create a “pull” on the water column. This pull results from the tendency of water molecules being evaporated on the surface of the plant to stay connected to water molecules below them, and so they are pulled along. Plants use this natural phenomenon to help transport water from their roots to their leaves. Without these properties of water, plants would be unable to receive the water and the dissolved minerals they require. In another example, insects such as the water strider,

shown in [\[link\]](#), use the surface tension of water to stay afloat on the surface layer of water and even mate there.



Water's cohesive and adhesive properties allow this water strider (*Gerris* sp.) to stay afloat. (credit: Tim Vickers)

Videos and additional links for additional information

If you are still having some difficulty with these concepts check out the following video links and web links on the properties of water

- [Hydrogen bonds refresher video](#).
- [water molecule polarity video](#).
- [Properties of water \(and its biological importance\)video](#).

Exercise:

Problem: The underlying basis of hydrogen bonding is:

- a. the tendency of a polar functional group to pick up a proton and become positively charged
- b. the ability of carbon to form four covalent bonds with hydrogen

- c. the unequal sharing of electrons by the strongly electronegative atoms O and N when they form covalent bonds, thus creating charge separation
 - d. the ability of a polar functional group to form an ionic bond with another polar functional group
 - e. the ability of a H bound to an electronegative atom to form an attraction with an electronegative atom of another compound
-

Solution:

e

Exercise:

Problem:

An ion dissolved in water is surrounded by a shell of water in which all of the water molecules orient their hydrogen atoms toward the ion; therefore, the ion is an anion.

- a. true
 - b. false
-

Solution:

a

Exercise:

Problem: What type of bonds must be broken for water to vaporize?

- a. non-polar covalent bonds
 - b. hydrogen bonds
 - c. hydrophobic interactions
 - d. ionic bonds
 - e. polar covalent bonds
-

Solution:

b

Exercise:

Problem: Which statement is true of the bonds in the water molecule?

- a. The bonds are ionic and no sharing of electrons occurs.
- b. Shared electrons spend more time around the hydrogen atoms.
- c. Shared electrons spend equal time around the oxygen and hydrogen atoms
- d. shared electrons spend more time around the oxygen atom
- e. A and D

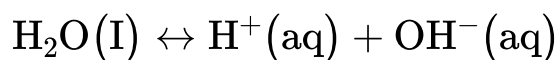
Solution:

D

pH, Buffers, Acids, and Bases

The pH of a solution indicates its acidity or alkalinity.

Equation:



litmus or pH paper, filter paper that has been treated with a natural water-soluble dye so it can be used as a pH indicator, to test how much acid (acidity) or base (alkalinity) exists in a solution. You might have even used some to test whether the water in a swimming pool is properly treated. In both cases, the pH test measures the concentration of hydrogen ions in a given solution.

Hydrogen ions are spontaneously generated in pure water by the dissociation (ionization) of a small percentage of water molecules into

equal numbers of hydrogen (H^+) ions and hydroxide (OH^-) ions. While the hydroxide ions are kept in solution by their hydrogen bonding with other water molecules, the hydrogen ions, consisting of naked protons, are immediately attracted to un-ionized water molecules, forming hydronium ions (H_3O^+). Still, by convention, scientists refer to hydrogen ions and their concentration as if they were free in this state in liquid water.

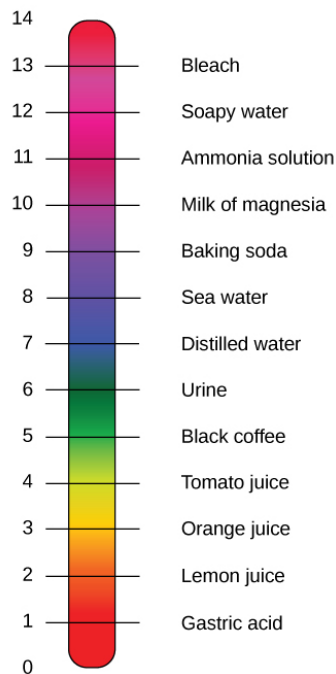
The concentration of hydrogen ions dissociating from pure water is 1×10^{-7} moles H^+ ions per liter of water. Moles (mol) are a way to express the amount of a substance (which can be atoms, molecules, ions, etc), with one mole being equal to 6.02×10^{23} particles of the substance. Therefore, 1 mole of water is equal to 6.02×10^{23} water molecules. The pH is calculated as the negative of the base 10 logarithm of this concentration. The \log_{10} of 1×10^{-7} is -7.0, and the negative of this number (indicated by the “p” of “pH”) yields a pH of 7.0, which is also known as neutral pH. The pH inside of human cells and blood are examples of two areas of the body where near-neutral pH is maintained.

Non-neutral pH readings result from dissolving acids or bases in water. Using the negative logarithm to generate positive integers, high concentrations of hydrogen ions yield a low pH number, whereas low levels of hydrogen ions result in a high pH. An **acid** is a substance that increases the concentration of hydrogen ions (H^+) in a solution, usually by having one of its hydrogen atoms dissociate. A **base** provides either hydroxide ions (OH^-) or other negatively charged ions that combine with hydrogen ions, reducing their concentration in the solution and thereby raising the pH. In cases where the base releases hydroxide ions, these ions bind to free hydrogen ions, generating new water molecules.

The stronger the acid, the more readily it donates H^+ . For example, hydrochloric acid (HCl) completely dissociates into hydrogen and chloride ions and is highly acidic, whereas the acids in tomato juice or vinegar do not completely dissociate and are considered weak acids. Conversely, strong bases are those substances that readily donate OH^- or take up hydrogen ions. Sodium hydroxide (NaOH) and many household cleaners are highly alkaline and give up OH^- rapidly when placed in water, thereby raising the pH. An example of a weak basic solution is seawater, which has

a pH near 8.0, close enough to neutral pH that marine organisms adapted to this saline environment are able to thrive in it.

The **pH scale** is, as previously mentioned, an inverse logarithm and ranges from 0 to 14 ([link](#)). Anything below 7.0 (ranging from 0.0 to 6.9) is acidic, and anything above 7.0 (from 7.1 to 14.0) is alkaline. Extremes in pH in either direction from 7.0 are usually considered inhospitable to life. The pH inside cells (6.8) and the pH in the blood (7.4) are both very close to neutral. However, the environment in the stomach is highly acidic, with a pH of 1 to 2. So how do the cells of the stomach survive in such an acidic environment? How do they homeostatically maintain the near neutral pH inside them? The answer is that they cannot do it and are constantly dying. New stomach cells are constantly produced to replace dead ones, which are digested by the stomach acids. It is estimated that the lining of the human stomach is completely replaced every seven to ten days.



The pH scale measures the concentration of hydrogen ions (H^+) in a solution.

(credit: modification of work
by Edward Stevens)

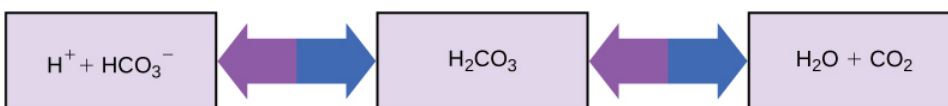
Note:

Link to Learning



Watch [this video](#) for a straightforward explanation of pH and its logarithmic scale.

So how can organisms whose bodies require a near-neutral pH ingest acidic and basic substances (a human drinking orange juice, for example) and survive? Buffers are the key. **Buffers** readily absorb excess H^+ or OH^- , keeping the pH of the body carefully maintained in the narrow range required for survival. Maintaining a constant blood pH is critical to a person's well-being. The buffer maintaining the pH of human blood involves carbonic acid (H_2CO_3), bicarbonate ion (HCO_3^-), and carbon dioxide (CO_2). When bicarbonate ions combine with free hydrogen ions and become carbonic acid, hydrogen ions are removed, moderating pH changes. Similarly, as shown in [\[link\]](#), excess carbonic acid can be converted to carbon dioxide gas and exhaled through the lungs. This prevents too many free hydrogen ions from building up in the blood and dangerously reducing the blood's pH. Likewise, if too much OH^- is introduced into the system, carbonic acid will combine with it to create bicarbonate, lowering the pH. Without this buffer system, the body's pH would fluctuate enough to put survival in jeopardy.



This diagram shows the body's buffering of blood pH levels. The blue arrows show the process of raising pH as more CO_2 is made. The purple arrows indicate the reverse process: the lowering of pH as more bicarbonate is created.

Other examples of buffers are antacids used to combat excess stomach acid. Many of these over-the-counter medications work in the same way as blood buffers, usually with at least one ion capable of absorbing hydrogen and moderating pH, bringing relief to those that suffer “heartburn” after eating. The unique properties of water that contribute to this capacity to balance pH—as well as water’s other characteristics—are essential to sustaining life on Earth.

Note:

Link to Learning



To learn more about water. Visit the [U.S. Geological Survey Water Science for Schools](https://www.usgs.gov/edu/water-science-for-schools) All About Water! website.

Additional Links

Here are some additional links on pH and pKa to help learn the material. Note that there is an additional module devoted to pKa.

Chemwiki Links

- [Determining and calculating pH](#)
- [Acid-Base titrations](#)
- [pH and pKa](#)

Khan Academy Links

- [What is pH](#)
- [strong acids and bases](#)
- [weak acids](#)
- [weak acid-base equilibria](#)
- [pH and pKa](#)

Simulations

- [Acid-base simulation.](#)
- [Intro to acids, bases, pH.](#)

Section Summary

Water has many properties that are critical to maintaining life. It is a polar molecule, allowing for the formation of hydrogen bonds. Hydrogen bonds allow ions and other polar molecules to dissolve in water. Therefore, water is an excellent solvent. The hydrogen bonds between water molecules cause the water to have a high heat capacity, meaning it takes a lot of added heat to raise its temperature. As the temperature rises, the hydrogen bonds between water continually break and form anew. This allows for the overall temperature to remain stable, although energy is added to the system. Water also exhibits a high heat of vaporization, which is key to how organisms cool themselves by the evaporation of sweat. Water's cohesive forces allow for the property of surface tension, whereas its adhesive properties are seen as water rises inside capillary tubes. The pH value is a measure of hydrogen ion concentration in a solution and is one of many chemical characteristics that is highly regulated in living organisms through homeostasis. Acids and

bases can change pH values, but buffers tend to moderate the changes they cause. These properties of water are intimately connected to the biochemical and physical processes performed by living organisms, and life would be very different if these properties were altered, if it could exist at all.

Review Questions

Exercise:

Problem: Which of the following statements is not true?

- a. Water is polar.
- b. Water stabilizes temperature.
- c. Water is essential for life.
- d. Water is the most abundant molecule in the Earth's atmosphere.

Solution:

D

Exercise:

Problem:

When acids are added to a solution, the pH should _____.

- a. decrease
- b. increase
- c. stay the same
- d. cannot tell without testing

Solution:

A

Exercise:

Problem:

A molecule that binds up excess hydrogen ions in a solution is called a(n) _____.

- a. acid
- b. isotope
- c. base
- d. donator

Solution:

C

Exercise:

Problem: Which of the following statements is true?

- a. Acids and bases cannot mix together.
- b. Acids and bases will neutralize each other.
- c. Acids, but not bases, can change the pH of a solution.
- d. Acids donate hydroxide ions (OH^-); bases donate hydrogen ions (H^+).

Solution:

B

Free Response**Exercise:**

Problem: Discuss how buffers help prevent drastic swings in pH.

Solution:

Buffers absorb the free hydrogen ions and hydroxide ions that result from chemical reactions. Because they can bond these ions, they prevent increases or decreases in pH. An example of a buffer system is the bicarbonate system in the human body. This system is able to absorb hydrogen and hydroxide ions to prevent changes in pH and keep cells functioning properly.

Exercise:

Problem: Why can some insects walk on water?

Solution:

Some insects can walk on water, although they are heavier (denser) than water, because of the surface tension of water. Surface tension results from cohesion, or the attraction between water molecules at the surface of the body of water (the liquid-air/gas interface).

Glossary

acid

molecule that donates hydrogen ions and increases the concentration of hydrogen ions in a solution

adhesion

attraction between water molecules and other molecules

base

molecule that donates hydroxide ions or otherwise binds excess hydrogen ions and decreases the concentration of hydrogen ions in a solution

buffer

substance that prevents a change in pH by absorbing or releasing hydrogen or hydroxide ions

calorie

amount of heat required to change the temperature of one gram of water by one degree Celsius

capillary action

occurs because water molecules are attracted to charges on the inner surfaces of narrow tubular structures such as glass tubes, drawing the water molecules to the sides of the tubes

cohesion

intermolecular forces between water molecules caused by the polar nature of water; responsible for surface tension

dissociation

release of an ion from a molecule such that the original molecule now consists of an ion and the charged remains of the original, such as when water dissociates into H^+ and OH^-

evaporation

separation of individual molecules from the surface of a body of water, leaves of a plant, or the skin of an organism

heat of vaporization of water

high amount of energy required for liquid water to turn into water vapor

hydrophilic

describes ions or polar molecules that interact well with other polar molecules such as water

hydrophobic

describes uncharged non-polar molecules that do not interact well with polar molecules such as water

litmus paper

(also, pH paper) filter paper that has been treated with a natural water-soluble dye that changes its color as the pH of the environment changes so it can be used as a pH indicator

pH paper

see litmus paper

pH scale

scale ranging from zero to 14 that is inversely proportional to the concentration of hydrogen ions in a solution

solvent

substance capable of dissolving another substance

specific heat capacity

the amount of heat one gram of a substance must absorb or lose to change its temperature by one degree Celsius

sphere of hydration

when a polar water molecule surrounds charged or polar molecules thus keeping them dissolved and in solution

surface tension

tension at the surface of a body of liquid that prevents the molecules from separating; created by the attractive cohesive forces between the molecules of the liquid

Bis2A 02.Appendix II Detailed look at Acid-Base Equilibrium

A more detailed look at Acid-Base chemistry

An important note about this module

This module is meant as an additional resource on Acid-Base chemistry to help further explain this critical process. It is much more mathematically intensive than the what was presented in Module 2.3 and is meant as a supplement. The purpose of providing this module is to help explain in more detail how the various equations and constants are derived. Use this module as a resource, it contains links to various videos and other resources that will help explain the basic concepts.

Acids and bases are very common substances whose properties vary greatly. Many acids are known to be quite corrosive, with the ability to dissolve solid metals or burn flesh. Many other acids, however, are not only benign but vital to the processes of life. Far from destroying biological molecules, they carry out reactions critical for organisms. Similarly, many bases are caustic cleansers while many others are medications to calm indigestion pains.

In this concept study, we will develop an understanding of the characteristics of molecules which make them either acids or bases. We will examine measurements about the relative strengths of acids and bases, and we will use these to develop a quantitative understanding of the relative strengths of acids and bases. From this, we can develop a qualitative understanding of the properties of molecules which determine whether a molecule is a strong acid or a weak acid, a strong base or a weak base. This understanding is valuable in predicting the outcomes of reactions, based on the relative quantitative strengths of acids and bases. These reactions are commonly referred to as neutralization reactions. A surprisingly large number of reactions, particularly in organic chemistry, can be understood as transfer of hydrogen ions from acid molecules to base molecules.

The point of this module is for you to become familiar with the concepts of acids and bases and how as biologist we use them in understanding how molecules interact with each other and the environment. You do not need to

memorize any equations or tables, but you should be able to use the tables and understand conceptually what is meant when we say, a specific carboxyl group has a pK_a of 2.2. Think of this as an extension to our discussion on water and pH; primarily because water can be thought of as an acid and a base. Remember that water can ionize into a hydroxyl ion (OH^-) and a Hydronium ion (H_3O^+), which is the basis for pH.

What is the role in Bis2A of acid-base chemistry

One basic concept of this course is that structure influences or drives function. That is how do molecules do what they do to allow for continued life. Much of this is based on what form of the molecule predominates. For example, as we will learn, the shape of protein is driven by the sequence of the amino acids and how they interact with each other. These interaction are influenced by the form many amino acids can take, whether they are protonated, in the basic form or deprotonated, in the acidic. Think about this would the protonated form of an acid or base effect how it interacts with other charged or uncharged compounds. For example, hemoglobin, the protein that carries oxygen in our blood is influenced by pH. The pH of the hemoglobin dictates whether it can bind or release oxygen.

Additional Links

Below you will find additional links that are meant to serve as supplemental material if you are having difficulty with this topic. These links go to the UC Davis Chemwiki site and videos from the Khan Academy.

Khan Academy Links

- [Acids and Bases.](#)

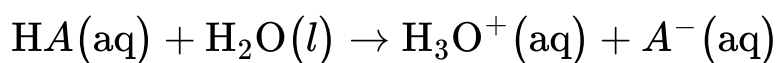
UCD Chemwiki links

- [acids and bases](#)
- [Bronsted acids and bases](#)

Observation 1: Strong Acids and Weak Acids

From the definition of an acid given in the Foundation, a typical acid can be written as HA, representing the hydrogen ion which will be donated and the rest of the molecule which will remain as a negative ion after the donation. The typical reaction of an acid in aqueous solution reacting with water can be written as

Equation:



In this reaction, HA(aq) represents an acid molecule dissolved in aqueous solution. $\text{H}_3\text{O}^+(\text{aq})$ is a notation to indicate that the donated proton has been dissolved in solution. Observations indicate that the proton is associated with several water molecules in a cluster, rather than attached to a single molecule. H_3O^+ is a simplified notation to represent this result. Similarly, the $\text{A}^-(\text{aq})$ ion is solvated by several water molecules. [\[link\]](#) is referred to as **acid ionization**.

[\[link\]](#) implies that a 0.1 M solution of the acid HA in water should produce H_3O^+ ions in solution with a concentration of 0.1M. In fact, the concentration of H_3O^+ ions, $[\text{H}_3\text{O}^+]$, can be measured by a variety of techniques. Chemists commonly use a measure of the H_3O^+ ion concentration called the pH, defined by:

$$\text{pH} = -\log [\text{H}_3\text{O}^+]$$

We now observe the concentration $[\text{H}_3\text{O}^+]$ produced by dissolving a variety of acids in solution at a concentration of 0.1 M, and the results are tabulated in [\[link\]](#).

Acid	$[\text{H}_3\text{O}^+]$ (M)	pH
------	------------------------------	----

Acid	[H ₃ O ⁺] (M)	pH
H ₂ SO ₄	0.1	1
HNO ₃	0.1	1
HCl	0.1	1
HBr	0.1	1
HI	0.1	1
HClO ₄	0.1	1
HClO ₃	0.1	1
HNO ₂	6.2×10^{-3}	2.2
HCN	7×10^{-6}	5.1
HIO	1×10^{-6}	5.8
HF	5.5×10^{-3}	2.3
HO-CN	5.5×10^{-3}	2.3
HClO ₂	2.8×10^{-2}	1.6
CH ₃ COOH (acetic acid)	1.3×10^{-3}	2.9
CH ₃ CH ₂ COOH (propionic acid)	1.1×10^{-3}	2.9

H₃O⁺ pH for 0.1 M Acid Solutions

Note that there are several acids listed for which [H₃O⁺] = 0.1 M, and pH. This shows that, for these acids, the acid ionization is complete: essentially every acid molecule is ionized in the solution according to [\[link\]](#). However,

there are other acids listed for which H_3O^+ is considerably less than 0.1M and the pH is considerably greater than 1. For each of these acids, therefore, not all of the acid molecules ionize according to [\[link\]](#). In fact, it is clear in [\[link\]](#) that in these acids the vast majority of the acid molecules do not ionize, and only a small percentage does ionize.

From these observations, we distinguish two classes of acids: **strong acids** and **weak acids**. Strong acids are those for which nearly 100% of the acid molecules ionize, whereas weak acids are those for which only a small percentage of molecules ionize. There are seven strong acids listed in [\[link\]](#). From many observations, it is possible to determine that these seven acids are the only commonly observed strong acids. The vast majority of all substances with acidic properties are weak acids. We seek to characterize weak acid ionization quantitatively and to determine what the differences in molecular properties are between strong acids and weak acids.

Observation 2: Percent Ionization in Weak Acids

[\[link\]](#) shows that the pH of 0.1 M acid solutions varies from one weak acid to another. If we dissolve 0.1 moles of acid in a 1.0 L solution, the fraction of those acid molecules which will ionize varies from weak acid to weak acid. For a few weak acids, using the data in [\[link\]](#) we calculate the percentage of ionized acid molecules in 0.1 M acid solutions in [\[link\]](#).

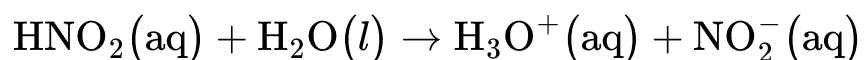
Acid	$[\text{H}_3\text{O}^+](\text{M})$	% ionization
HNO_2	6.2×10^{-3}	6.2%
HCN	7×10^{-6}	0.007%
HIO	1×10^{-6}	0.001%

Acid	$[\text{H}_3\text{O}^+](\text{M})$	% ionization
HF	5.5×10^{-3}	5.5%
HOCN	5.5×10^{-3}	5.5%
HClO_2	2.8×10^{-2}	28.2%
CH_3COOH (acetic acid)	1.3×10^{-3}	1.3%
$\text{CH}_3\text{CH}_2\text{COOH}$ (propionic acid)	1.1×10^{-3}	1.1%

Percent Ionization of 0.1 M Acid Solutions

We might be tempted to conclude from [\[link\]](#) that we can characterize the strength of each acid by the percent ionization of acid molecules in solution. However, before doing so, we observe the pH of a single acid, nitrous acid, in solution as a function of the concentration of the acid.

Equation:



In this case, "concentration of the acid" refers to the number of moles of acid that we dissolved per liter of water. Our observations are listed in [\[link\]](#), which gives $[\text{H}_3\text{O}^+]$, pH, and percent ionization as a function of nitrous acid concentration.

$c_0 (\text{M})$	$[\text{H}_3\text{O}^+]$	pH	% Ionization
0.50	1.7×10^{-2}	1.8	3.3%

c_0 (M)	$[\text{H}_3\text{O}^+]$	pH	% Ionization
0.20	1.0×10^{-2}	2.0	5.1%
0.10	7.0×10^{-3}	2.2	7.0%
0.050	4.8×10^{-3}	2.3	9.7%
0.020	2.9×10^{-3}	2.5	14.7%
0.010	2.0×10^{-3}	2.7	20.0%
0.005	1.3×10^{-3}	2.9	26.7%
0.001	4.9×10^{-4}	3.3	49.1%
0.0005	3.0×10^{-4}	3.5	60.8%

% Ionization of Nitrous Acid

Surprisingly, perhaps, the percent ionization varies considerably as a function of the concentration of the nitrous acid. We recall that this means that the fraction of molecules which ionize, according to [\[link\]](#), depends on how many acid molecules there are per liter of solution. Since some but not all of the acid molecules are ionized, this means that nitrous acid molecules are present in solution at the same time as the negative nitrite ions and the positive hydrogen ions. Recalling our observation of equilibrium in gas phase reactions, we can conclude that [\[link\]](#) achieves equilibrium for each concentration of the nitrous acid.

Since we know that gas phase reactions come to equilibrium under conditions determined by the equilibrium constant, we might speculate that the same is true of reactions in aqueous solution, including acid ionization. We therefore define an analogy to the gas phase reaction equilibrium constant. In this case, we would not be interested in the pressures of the

components, since the reactants and products are all in solution. Instead, we try a function composed of the equilibrium concentrations:

Equation:

$$K = \frac{[\text{H}_3\text{O}^+][\text{NO}_2^-]}{[\text{HNO}_2][\text{H}_2\text{O}]}$$

The concentrations at equilibrium can be calculated from the data in [\[link\]](#) for nitrous acid. $[\text{H}_3\text{O}^+]$ is listed and $[\text{NO}_2^-] = [\text{H}_3\text{O}^+]$. Furthermore, if c_0 is the initial concentration of the acid defined by the number of moles of acid dissolved in solution per liter of solution, then $\text{HA} = c_0 - [\text{H}_3\text{O}^+]$. Note that the contribution of $[\text{H}_2\text{O}(l)]$ to the value of the function K is simply a constant. This is because the "concentration" of water in the solution is simply the molar density of water, $\frac{n_{\text{H}_2\text{O}}}{V} = 55.5M$, which is not affected by the presence or absence of solute. All of the relevant concentrations, along with the function in [\[link\]](#) are calculated and tabulated in [\[link\]](#).

c_0 (M)	$[\text{H}_3\text{O}^+]$	$[\text{NO}_2^-]$	$[\text{HNO}_2]$	K
0.50	1.7×10^{-2}	1.7×10^{-2}	0.48	1.0×10^{-5}
0.20	1.0×10^{-2}	1.0×10^{-2}	0.19	9.9×10^{-6}
0.10	7.0×10^{-3}	7.0×10^{-3}	9.3×10^{-2}	9.6×10^{-6}
0.050	4.8×10^{-3}	4.8×10^{-3}	4.5×10^{-2}	9.4×10^{-6}
0.020	2.9×10^{-3}	2.9×10^{-3}	4.5×10^{-2}	9.4×10^{-6}
0.010	2.0×10^{-3}	2.0×10^{-3}	8.0×10^{-3}	8.9×10^{-6}

c_0 (M)	$[\text{H}_3\text{O}^+]$	$[\text{NO}_2^-]$	$[\text{HNO}_2]$	K
0.005	1.3×10^{-3}	1.3×10^{-3}	3.6×10^{-3}	8.8×10^{-6}
0.001	4.9×10^{-4}	4.9×10^{-4}	5.1×10^{-4}	8.5×10^{-6}
0.0005	3.0×10^{-4}	3.0×10^{-4}	2.0×10^{-4}	8.5×10^{-6}

Equilibrium Concentrations and K for Nitrous Acid

We note that the function K in [\[link\]](#) is approximately, though only approximately, the same for all conditions analyzed in [\[link\]](#). Variation of the concentration by a factor of 1000 produces a change in K of only 10% to 15%. Hence, we can regard the function K as a constant which approximately describes the acid ionization equilibrium for nitrous acid. By convention, chemists omit the constant concentration of water from the equilibrium expression, resulting in the **acid ionization equilibrium constant**, K_a , defined as:

Equation:

$$K_a = \frac{[\text{H}_3\text{O}^+][\text{NO}_2^-]}{[\text{HNO}_2]}$$

From an average of the data in [\[link\]](#), we can calculate that, at 25°C for nitrous acid, $K_a = 5 \times 10^{-4}$. Acid ionization constants for the other weak acids in [\[link\]](#) are listed in [\[link\]](#).

Acid	K_a	$\text{p}K_a$
HNO_2	5×10^{-4}	3.3

Acid	K_a	pK_a
HCN	4.9×10^{-10}	9.3
HIO	2.3×10^{-11}	10.6
HF	3.5×10^{-4}	3.4
HOCN	3.5×10^{-4}	3.4
HClO ₂	1.1×10^{-2}	2.0
CH ₃ COOH(acetic acid)	1.7×10^{-5}	4.8
CH ₃ CH ₂ COOH(propionic acid)	1.4×10^{-5}	4.9

Weak Acid Ionization Constants, K_a and pK_a

We make two final notes about the results in [\[link\]](#). First, it is clear the larger the value of K_a , the stronger the acid. That is, when K_a is a larger number, the percent ionization of the acid is larger, and vice versa. Second, the values of K_a vary over many orders of magnitude. As such, it is often convenient to define the quantity pK_a , analogous to pH, for purposes of comparing acid strengths:

Equation:

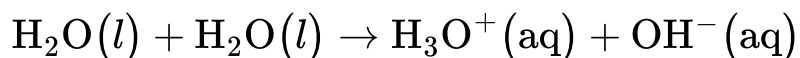
$$pK_a = -\log K_a$$

The value of pK_a for each acid is also listed in [\[link\]](#). Note that a small value of pK_a implies a large value of K_a and thus a stronger acid. Weaker acids have larger values of pK_a . K_a and pK_a thus give a simple quantitative comparison of the strength of weak acids.

Observation 3: Autoionization of Water

Since we have the ability to measure pH for acid solutions, we can measure pH for pure water as well. It might seem that this would make no sense, as we would expect $[\text{H}_3\text{O}^+]$ to equal zero exactly in pure water. Surprisingly, this is incorrect: a measurement on pure water at 25°C yields pH, so that $[\text{H}_3\text{O}^+] = 1.0 \times 10^{-7} \text{ M}$. There can be only one possible source for these ions: water molecules. The process

Equation:



is referred to as the **autoionization** of water. Note that, in this reaction, some water molecules behave as acid, donating protons, while other water molecules behave as base, accepting protons.

Since at equilibrium $[\text{H}_3\text{O}^+] = 1.0 \times 10^{-7} \text{ M}$, it must also be true that $[\text{OH}^-] = 1.0 \times 10^{-7} \text{ M}$. We can write the equilibrium constant for [\[link\]](#), following our previous convention of omitting the pure water from the expression, and we find that, at 25°C,

Equation:

$$\begin{aligned} K_w &= [\text{H}_3\text{O}^+][\text{OH}^-] \\ &= 1.0 \times 10^{-14} \text{ M} \end{aligned}$$

(In this case, the subscript "w" refers to "water".)

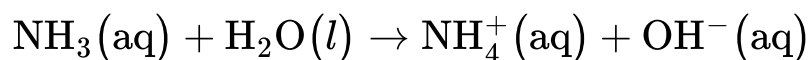
[\[link\]](#) occurs in pure water but must also occur when ions are dissolved in aqueous solutions. This includes the presence of acids ionized in solution. For example, we consider a solution of 0.1M acetic acid. Measurements show that, in this solution $[\text{H}_3\text{O}^+] = 1.3 \times 10^{-3} \text{ M}$ and $[\text{OH}^-] = 7.7 \times 10^{-12} \text{ M}$. We note two things from this observation: first, the value of $[\text{OH}^-]$ is considerably less than in pure water; second, the autoionization equilibrium constant remains the same at 1.0×10^{-14} . From these notes, we can conclude that the autoionization equilibrium of water occurs in acid solution, but the extent of autoionization is suppressed by the presence of the acid in solution.

We consider a final note on the autoionization of water. The pH of pure water is 7 at 25°C. Adding any acid to pure water, no matter how weak the acid, must increase $[\text{H}_3\text{O}^+]$, thus producing a pH below 7. As such, we can conclude that, for all acid solutions, pH is less than 7, or on the other hand, any solution with pH less than 7 is acidic.

Observation 4: Base Ionization, Neutralization and Hydrolysis of Salts

We have not yet examined the behavior of base molecules in solution, nor have we compared the relative strengths of bases. We have defined a base molecule as one which accepts a positive hydrogen ion from another molecule. One of the most common examples is ammonia, NH_3 . When ammonia is dissolved in aqueous solution, the following reaction occurs:

Equation:



Due to the lone pair of electrons on the highly electronegative N atom, NH_3 molecules will readily attach a free hydrogen ion forming the ammonium ion NH_4^+ . When we measure the concentration of OH^- for various initial concentration of NH_3 in water, we observe the results in [\[link\]](#). We should anticipate that a base ionization equilibrium constant might exist comparable to the acid ionization equilibrium constant, and in [\[link\]](#), we have also calculated the value of the function K_b defined as:

Equation:

$$K_b = \frac{[\text{NH}_4^+][\text{OH}^-]}{[\text{NH}_3]}$$

C₀(M)	[OH⁻]	K_b	pH
0.50	3.2×10^{-3}	2.0×10^{-5}	11.5
0.20	2.0×10^{-3}	2.0×10^{-5}	11.3
0.10	1.4×10^{-3}	2.0×10^{-5}	11.1
0.050	9.7×10^{-4}	1.9×10^{-5}	11.0
0.020	6.0×10^{-4}	1.9×10^{-5}	10.8
0.010	4.2×10^{-4}	1.9×10^{-5}	10.6
0.005	3.0×10^{-4}	1.9×10^{-5}	10.5
0.001	1.3×10^{-4}	1.8×10^{-5}	10.1
0.0005	8.7×10^{-5}	1.8×10^{-5}	9.9

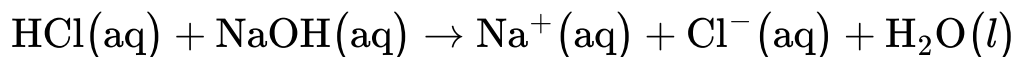
Equilibrium Concentrations and K_b for Ammonia

Given that we have dissolved a base in pure water, we might be surprised to discover the presence of positive hydrogen ions, H₃O⁺, in solution, but a measurement of the pH for each of the solutions reveals small amounts. The pH for each solution is also listed in [\[link\]](#). The source of these H₃O⁺ ions must be the autoionization of water. Note, however, that in each case in basic solution, the concentration of H₃O⁺ ions is less than that in pure water. Hence, the presence of the base in solution has suppressed the autoionization. Because of this, in each case the pH of a basic solution is greater than 7.

Base ionization is therefore quite analogous to acid ionization observed earlier. We now consider a comparison of the strength of an acid to the strength of a base. To do so, we consider a class of reactions called "neutralization reactions" which occur when we mix an acid solution with a base solution. Since the acid donates protons and the base accepts protons,

we might expect, when mixing acid and base, to achieve a solution which is no longer acidic or basic. For example, if we mix together equal volumes of 0.1M HCl(aq) and 0.1M NaOH(aq), the following reaction occurs:

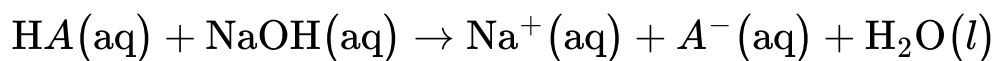
Equation:



The resultant solution is simply a salt solution with NaCl dissolved in water. This solution has neither acidic nor basic properties, and the pH is 7; hence the acid and base have neutralized each other. In this case, we have mixed together a strong acid with a strong base. Since both are strong and since we mixed equal molar quantities of each, the neutralization reaction is essentially complete.

We next consider mixing together a weak acid solution with a strong base solution, again with equal molar quantities of acid and base. As an example, we mix 100ml of 0.1M acetic acid (HA) solution with 100ml of 0.1M sodium hydroxide. In this discussion, we will abbreviate the acetic acid molecular formula CH_3COOH as HA and the acetate ion CH_3COO^- as A^- . The reaction of HA and NaOH is:

Equation:

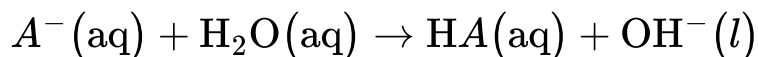


$\text{A}^-(\text{aq})$ is the acetate ion in solution, formed when an acetic acid molecule donates the positive hydrogen ion. We have thus created a salt solution again, in this case of sodium acetate in water. Note that the volume of the combined solution is 200ml, so the concentration of sodium acetate (NaA) in solution is 0.050M.

Unlike our previous NaCl salt solution, a measurement in this case reveals that the pH of the product salt solution is 9.4, so the solution is basic. Thus, mixing equal molar quantities of strong base with weak acid produces a basic solution. In essence, the weak acid does not fully neutralize the strong base. To understand this, we examine the behavior of sodium acetate in solution. Since the pH is greater than 7, then there is an excess of OH^- ions

in solution relative to pure water. These ions must have come from the reaction of sodium acetate with the water. Therefore, the negative acetate ions in solution must behave as a base, accepting positive hydrogen ions:

Equation:



The reaction of an ion with water to form either an acid or a base solution is referred to as **hydrolysis**. From this example, the salt of a weak acid behaves as a base in water, resulting in a pH greater than 7.

To understand the extent to which the hydrolysis of the negative ion occurs, we need to know the equilibrium constant for this reaction. This turns out to be determined by the acid ionization constant for HA. To see this, we write the equilibrium constant for the hydrolysis of A^{-} as

Equation:

$$K_h = \frac{[\text{HA}] [\text{OH}^{-}]}{[A^{-}]}$$

Multiplying numerator and denominator by $[\text{H}_3\text{O}^{+}]$, we find that

Equation:

$$\begin{aligned} K_h &= \frac{[\text{HA}][\text{OH}^{-}]}{[A^{-}]} \frac{[\text{H}_3\text{O}^{+}]}{[\text{H}_3\text{O}^{+}]} \\ &= \frac{K_w}{K_a} \end{aligned}$$

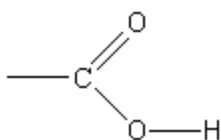
Therefore, for the hydrolysis of acetate ions in solution, $K_h = 5.8 \times 10^{-10}$. This is fairly small, so the acetate ion is a very weak base.

Observation 5: Acid strength and molecular properties

We now have a fairly complete quantitative description of acid-base equilibrium. To complete our understanding of acid-base equilibrium, we

need a predictive model which relates acid strength or base strength to molecular properties. In general, we expect that the strength of an acid is related either to the relative ease by which it can donate a hydrogen ion or by the relative stability of the remaining negative ion formed after the departure of the hydrogen ion.

To begin, we note that there are three basic categories of acids which we have examined in this study. First, there are simple **binary acids**: HF HCl HBr HI. Second, there are acids formed from main group elements combined with one or more oxygen atoms, such H₂SO₄ or HNO₃. These are called **oxyacids**. Third, there are the **carboxylic acids**, organic molecules which contain the carboxylic functional group in [\[link\]](#).



Carboxyli
c
Functional
Group

We consider first the simple binary acids. HCl, HBr, and HI are all strong acids, whereas HF is a weak acid. In comparing the experimental values of pK_a values in [\[link\]](#), we note that the acid strength increases in the order HF < HCl < HBr < HI. This means that the hydrogen ion can more readily separate from the covalent bond with the halogen atom (X) as we move down the periodic table. This is reasonable, because the strength of the H-X bond also decreases as we move down the periodic table, as shown in [\[link\]](#).

	pK_a	Bond Energy ($\frac{\text{kJ}}{\text{mol}}$)
HF	3.1	567.7
HCl	-6.0	431.6
HBr	-9.0	365.9
HI	-9.5	298.0

H-X Bond Strengths and pK_a

The decreasing strength of the H-X bond is primarily due to the increase in the size of the X atom as we move down the periodic table. We conclude that one factor which influences acidity is the strength of the H-X bond: a weaker bond produces a stronger acid, and vice versa.

In the acids in the other two categories, the hydrogen atom which ionizes is attached directly to an oxygen atom. Thus, to understand acidity in these molecules, we must examine what the oxygen atom is in turn bonded to. It is very interesting to note that, in examining compounds like R-O-H, where R is an atom or group of atoms, we can get either acidic or basic properties. For examples, NaOH is a strong base, whereas HOCl is a weak acid. This means that, when NaOH ionizes in solution, the Na-O linkage ionizes, whereas when HOCl ionizes in solution, the H-O bond ionizes.

To understand this behavior, we compare the strength of the simple oxyacids HOI, HOBr, and HOCl. The pK_a 's for these acids are found experimentally to be, respectively, 10.6, 8.6, and 7.5. The acid strength for HOX increases as we move up the periodic table in the halogen group. This means that the H-O bond ionizes more readily when the oxygen atom is bonded to a more electronegative atom.

We can add to this observation by comparing the strengths of the acids HOCl, HOClO, HOClO₂, and HOClO₃. (Note that the molecular formulae are more commonly written as HClO, HClO₂, HClO₃, and HClO₄. We have written them instead to emphasize the molecular structure.) The pK_a 's of

these acids are, respectively, 7.5, 2.0, -2.7, and -8.0. In each case, the molecule with more oxygen atoms on the central Cl atom is the stronger acid: HOClO is more acidic than HOCl , etc. A similar result is found in comparing the oxyacids of nitrogen. HONO_2 , nitric acid, is one of the strong acids, whereas HONO , nitrous acid, is a weak acid. Since oxygen atoms are very strongly electronegative, these trends add to our observation that increasing electronegativity of the attached atoms increases the ionization of the O-H bond.

Why would electronegativity play a role in acid strength? There are two conclusions we might draw. First, a greater electronegativity of the atom or atoms attached to the H-O in the oxyacid apparently results in a weaker H-O bond, which is thus more readily ionized. We know that an electronegative atom polarizes bonds by drawing the electrons in the molecule towards it. In this case, the Cl in HOCl and the Br in HOBr must polarize the H-O bond, weakening it and facilitating the ionization of the hydrogen. In comparing HOCl to HOClO , the added oxygen atom must increase the polarization of the H-O bond, thus weakening the bond further and increasing the extent of ionization.

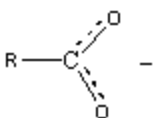
A second conclusion has to do with the ion created by the acid ionization. The negative ion produced has a surplus electron, and the relative energy of this ion will depend on how readily that extra electron is attracted to the atoms of ion. The more electronegative those atoms are, the stronger is the attraction. Therefore, the OCl^- ion can more readily accommodate the negative charge than can the OBr^- ion. And the OClO^- ion can more readily accommodate the negative charge than can the OCl^- ion.

We conclude that the presence of strongly electronegative atoms in an acid increases the polarization of the H-O bond, thus facilitating ionization of the acid, and increases the attraction of the extra electron to the negative ion, thus stabilizing the negative ion. Both of these factors increase the acid strength. Chemists commonly use both of these conclusions in understanding and predicting relative acid strength.

The relative acidity of carbon compounds is a major subject of organic chemistry, which we can only visit briefly here. In each of the carboxylic acids, the H-O group is attached to a carbonyl C=O group, which is in turn

bonded to other atoms. The comparison we observe here is between carboxylic acid molecules, denoted as RCOOH , and other organic molecules containing the H-O group, such as alcohols denoted as ROH . (R is simply an atom or group of atoms attached to the functional group.) The former are obviously acids whereas the latter group contains molecules which are generally extremely weak acids. One interesting comparison is for the acid and alcohol when R is the benzene ring, C_6H_5 . Benzoic acid, $\text{C}_6\text{H}_5\text{COOH}$, has $pK_a = 4.2$, whereas phenol, $\text{C}_6\text{H}_5\text{OH}$, has $pK_a = 9.9$. Thus, the presence of the doubly bonded oxygen atom on the carbon atom adjacent to the O-H clearly increases the acidity of the molecule, and thus increases ionization of the O-H bond.

This observation is quite reasonable in the context of our previous conclusion. Adding an electronegative oxygen atom in near proximity to the O-H bond both increases the polarization of the O-H bond and stabilizes the negative ion produced by the acid ionization. In addition to the electronegativity effect, carboxylate anions, RCOO^- , exhibit resonance stabilization, as seen in [\[link\]](#).



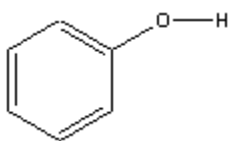
The resonance results in a sharing of the negative charge over several atoms, thus stabilizing the negative ion. This is a major contributing factor in the acidity of carboxylic acids versus alcohols.

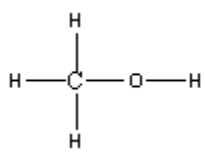
Review and Discussion Questions

1. Strong acids have a higher percent ionization than do weak acids. Why don't we use percent ionization as a measure of acid strength, rather than K_a ?
2. Using the data in [\[link\]](#) for nitrous acid, plot $[\text{H}_3\text{O}^+]$ versus c_0 , the initial concentration of the acid, and versus $[\text{HNO}_2]$ the equilibrium concentration of the acid. On a second graph, plot $[\text{H}_3\text{O}^+]^2$ versus c_0 , the initial concentration of the acid, and versus $[\text{HNO}_2]$ the

- equilibrium concentration of the acid. Which of these results gives a straight line? Using the equilibrium constant expression, explain your answer.
- Using Le Châtelier's principle, explain why the concentration of $[\text{OH}^-]$ is much lower in acidic solution than it is in neutral solution.
 - We considered mixing a strong base with a weak acid, but we did not consider mixing a strong acid with a weak acid. Consider mixing 0.1M HNO_3 and 0.1M HNO_2 . Predict the pH of the solution and the percent ionization of the nitrous acid. Rationalize your prediction using Le Châtelier's principle.
 - Imagine taking a 0.5M solution of nitrous acid and slowly adding water to it. Looking at [\[link\]](#), we see that, as the concentration of nitrous acid decreases, the percent ionization increases. By contrast, $[\text{H}_3\text{O}^+]$ decreases. Rationalize these results using Le Châtelier's principle.
 - We observed that mixing a strong acid and a strong base, in equal amounts and concentrations, produces a neutral solution, and that mixing a strong base with a weak acid, in equal amounts and concentrations, produces a basic solution. Imagine mixing a weak acid and a weak base, in equal amounts and concentrations. Predict whether the resulting solution will be acidic, basic, or neutral, and explain your prediction.
 - Using the electronegativity arguments presented [above](#), explain why, in general, compounds like M-O-H are bases rather than acids, when M is a metal atom. Predict the relationship between the properties of the metal atom M and the strength of the base MOH.
 - Ionization of sulfuric acid H_2SO_4 produces HSO_4^- , which is also an acid. However, HSO_4^- is a much weaker acid than H_2SO_4 . Using the conclusions from [above](#), explain why HSO_4^- is a much weaker acid.
 - Predict and explain the relative acid strengths of H_2S and HCl . Predict and explain the relative acid strengths of H_3PO_4 and H_3AsO_4 .
 - Using arguments from [above](#), predict and explain the relative acidity of [phenol](#) and [methanol](#).

Phenol





Methanol

Bis2A 03.0 Introduction to Macromolecules

class="introduction"

Foods such as
bread, fruit, and
cheese are rich
sources of
biological
macromolecules
. (credit:
modification of
work by Bengt
Nyman)



Food provides the body with the nutrients it needs to survive. Many of these critical nutrients are biological macromolecules, or large molecules, necessary for life. These macromolecules (polymers) are built from

different combinations of smaller organic molecules (monomers). What specific types of biological macromolecules do living things require? How are these molecules formed? What functions do they serve? In this chapter, these questions will be explored.

Specifically we will address the four classes of macromolecules that compose all living cells: **Proteins**, **Carbohydrates**, **Lipids**, and **nucleic acids**.

video links

To help put this topic into perspective in a rather amusing way, is a video entitled: [Biological Molecules - You Are What You Eat: Crash Course Biology #3](#). The video is 14 minutes in length and provides some of the basics in a rather enjoyable way Enjoy.

Bis2A 03.1 Proteins v1.2

By the end of this section, you will be able to:

- Describe the functions proteins perform in the cell and in tissues
- Discuss the relationship between amino acids and proteins
- Explain the four levels of protein organization
- Describe the ways in which protein shape and function are linked

Proteins are one of the most abundant organic molecules in living systems and have the most diverse range of functions of all macromolecules.

Proteins may be structural, regulatory, contractile, or protective; they may serve in transport, storage, or membranes; or they may be toxins or enzymes. Each cell in a living system may contain thousands of proteins, each with a unique function. Their structures, like their functions, vary greatly. They are all, however, polymers of amino acids, arranged in a linear sequence.

Types and Functions of Proteins

Enzymes, which are produced by living cells, are catalysts in biochemical reactions (like digestion) and are usually complex or conjugated proteins. Each enzyme is specific for the substrate (a reactant that binds to an enzyme) it acts on. The enzyme may help in breakdown, rearrangement, or synthesis reactions. Enzymes that break down their substrates are called catabolic enzymes, enzymes that build more complex molecules from their substrates are called anabolic enzymes, and enzymes that affect the rate of reaction are called catalytic enzymes. It should be noted that all enzymes increase the rate of reaction and, therefore, are considered to be organic catalysts. An example of an enzyme is salivary amylase, which hydrolyzes its substrate amylose, a component of starch.

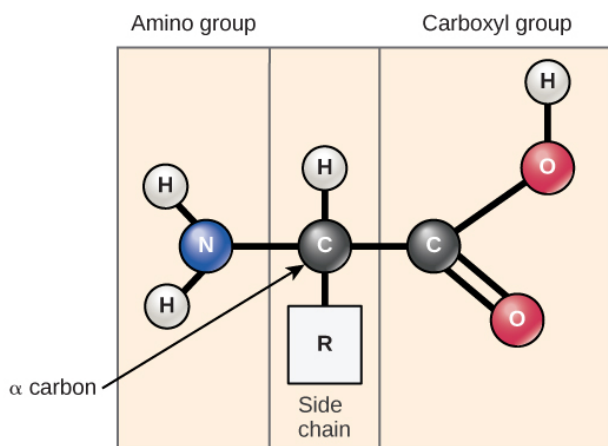
Hormones are chemical-signaling molecules, usually small proteins or steroids, secreted by endocrine cells that act to control or regulate specific physiological processes, including growth, development, metabolism, and reproduction. For example, insulin is a protein hormone that helps to regulate the blood glucose level. The primary types and functions of proteins are listed in [\[link\]](#).

Protein Types and Functions		
Type	Examples	Functions
Digestive Enzymes	Amylase, lipase, pepsin, trypsin	Help in digestion of food by catabolizing nutrients into monomeric units
Transport	Hemoglobin, albumin	Carry substances in the blood or lymph throughout the body
Structural	Actin, tubulin, keratin	Construct different structures, like the cytoskeleton
Hormones	Insulin, thyroxine	Coordinate the activity of different body systems
Defense	Immunoglobulins	Protect the body from foreign pathogens
Contractile	Actin, myosin	Effect muscle contraction
Storage	Legume storage proteins, egg white (albumin)	Provide nourishment in early development of the embryo and the seedling

Proteins have different shapes and molecular weights; some proteins are globular in shape whereas others are fibrous in nature. For example, hemoglobin is a globular protein, but collagen, found in our skin, is a fibrous protein. Protein shape is critical to its function, and this shape is maintained by many different types of chemical bonds. Changes in temperature, pH, and exposure to chemicals may lead to permanent changes in the shape of the protein, leading to loss of function, known as **denaturation**. All proteins are made up of different arrangements of the same 20 types of amino acids.

Amino Acids

Amino acids are the monomers that make up proteins. Each amino acid has the same fundamental structure, which consists of a central carbon atom, also known as the alpha (α) carbon, bonded to an amino group (NH_2), a carboxyl group (COOH), and to a hydrogen atom. Every amino acid also has another atom or group of atoms bonded to the central atom known as the R group ([\[link\]](#)). For an introduction on amino acids, click [here](#) for a short(4 minute) video.



Amino acids have a central asymmetric carbon to which an amino group, a carboxyl group, a hydrogen atom, and a side chain (R group) are attached.

The name "amino acid" is derived from the fact that they contain both amino group and carboxyl-acid-group in their basic structure. As mentioned, there are 20 amino acids present in proteins. Ten of these are considered essential amino acids in humans because the human body cannot produce them and they are obtained from the diet. For each amino acid, the R group (or side chain) is different ([\[link\]](#)).

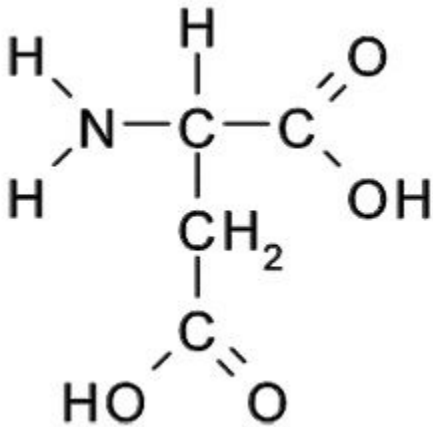
Exercise:**Problem:**

Using figure 2.1, which of the following is true about amino acids:

- a. amino acids contain polar functional groups
- b. amino acids contain basic functional groups
- c. amino acids contain acidic functional groups
- d. amino acids contain a variable group that can be either polar or nonpolar
- e. all of the above

Solution:

e



The chemical structure
of Aspartic acid
(Aspartate)

Exercise:

Problem:

Using the figure of Aspartic acid (an amino acid) above in Figure 2.2:

- a. This amino acid is polar
- b. This amino acid is nonpolar
- c. This amino acid is hydrophilic
- d. this amino acid is hydrophobic
- e. a and c
- f. b and d

Solution:

e

Note:

Art Connection

AMINO ACID			
Nonpolar, aliphatic R groups			
	Glycine	Alanine	Valine
	Leucine	Methionine	Isoleucine
	Serine	Threonine	Cysteine
Polar, uncharged R groups			
	Proline	Asparagine	Glutamine
AMINO ACID			
Positively charged R groups			
	Lysine	Arginine	Histidine
Negatively charged R groups			
	Aspartate	Glutamate	
Nonpolar, aromatic R groups			
	Phenylalanine	Tyrosine	Tryptophan

There are 20 common amino acids commonly found in proteins, each with a different R group (variant group) that determines its chemical nature.

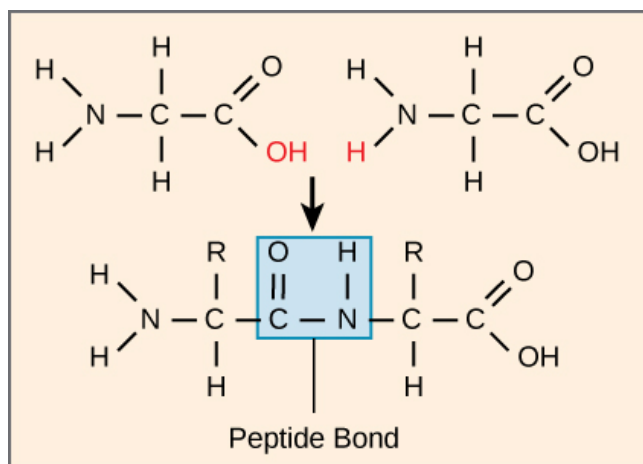
Which categories of amino acid would you expect to find on the surface of a soluble protein, and which would you expect to find in the interior? What distribution of amino acids would you expect to find in a protein embedded in a lipid bilayer?

The chemical nature of the side chain determines the nature of the amino acid (that is, whether it is acidic, basic, polar, or nonpolar). For example, the amino acid glycine has a hydrogen atom as the R group. Amino acids such as valine, methionine, and alanine are nonpolar or hydrophobic in nature,

while amino acids such as serine, threonine, and cysteine are polar and have hydrophilic side chains. The side chains of lysine and arginine are positively charged, and therefore these amino acids are also known as basic amino acids. Proline has an R group that is linked to the amino group, forming a ring-like structure. Proline is an exception to the standard structure of an amino acid since its amino group is not separate from the side chain ([\[link\]](#)).

Amino acids are represented by a single upper case letter or a three-letter abbreviation. For example, valine is known by the letter V or the three-letter symbol val. Just as some fatty acids are essential to a diet, some amino acids are necessary as well. They are known as essential amino acids, and in humans they include isoleucine, leucine, and cysteine. Essential amino acids refer to those necessary for construction of proteins in the body, although not produced by the body; which amino acids are essential varies from organism to organism.

The sequence and the number of amino acids ultimately determine the protein's shape, size, and function. Each amino acid is attached to another amino acid by a covalent bond, known as a **peptide bond**, which is formed by a dehydration reaction. The carboxyl group of one amino acid and the amino group of the incoming amino acid combine, releasing a molecule of water. The resulting bond is the peptide bond ([\[link\]](#)).



Peptide bond formation is a

dehydration synthesis reaction.
The carboxyl group of one amino acid is linked to the amino group of the incoming amino acid. In the process, a molecule of water is released.

Exercise:

Problem: Where do peptide bonds form?

- a. between the carboxyl group of one amino acid and the amino group of another amino acid
- b. between the adjacent carboxyl groups on amino acids
- c. between amino acids of two different protein chains
- d. between adjacent amino groups on amino acids
- e. a and c
- f. c and d

Solution:

a

The products formed by such linkages are called peptides. As more amino acids join to this growing chain, the resulting chain is known as a polypeptide. Each polypeptide has a free amino group at one end. This end is called the N terminal, or the amino terminal, and the other end has a free carboxyl group, also known as the C or carboxyl terminal. While the terms polypeptide and protein are sometimes used interchangeably, a polypeptide is technically a polymer of amino acids, whereas the term protein is used for a polypeptide or polypeptides that have combined together, often have bound non-peptide prosthetic groups, have a distinct shape, and have a unique function. After protein synthesis (translation), most proteins are modified. These are known as post-translational modifications. They may undergo cleavage, phosphorylation, or may require the addition of other

chemical groups. Only after these modifications is the protein completely functional.

Note:

Link to Learning



Click through the steps of protein synthesis in this [interactive tutorial](#).

Note:

Evolution Connection

The Evolutionary Significance of Cytochrome c

Cytochrome c is an important component of the electron transport chain, a part of cellular respiration, and it is normally found in the cellular organelle, the mitochondrion. This protein has a heme prosthetic group, and the central ion of the heme gets alternately reduced and oxidized during electron transfer. Because this essential protein's role in producing cellular energy is crucial, it has changed very little over millions of years. Protein sequencing has shown that there is a considerable amount of cytochrome c amino acid sequence homology among different species; in other words, evolutionary kinship can be assessed by measuring the similarities or differences among various species' DNA or protein sequences.

Scientists have determined that human cytochrome c contains 104 amino acids. For each cytochrome c molecule from different organisms that has been sequenced to date, 37 of these amino acids appear in the same position in all samples of cytochrome c. This indicates that there may have

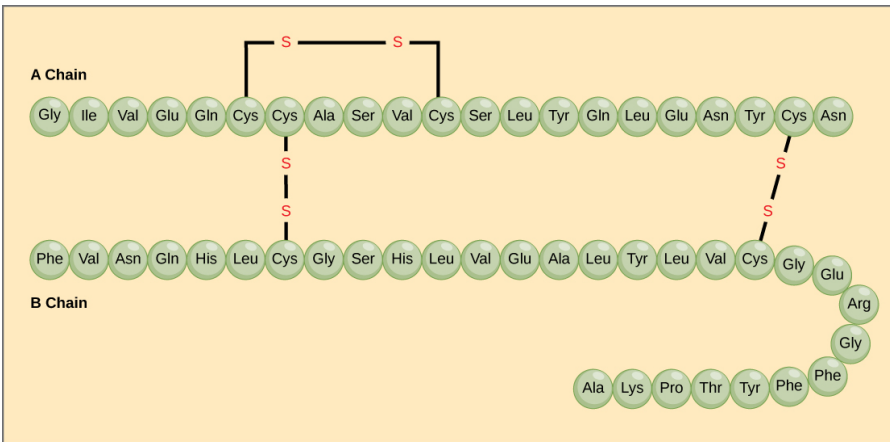
been a common ancestor. On comparing the human and chimpanzee protein sequences, no sequence difference was found. When human and rhesus monkey sequences were compared, the single difference found was in one amino acid. In another comparison, human to yeast sequencing shows a difference in the 44th position.

Protein Structure

As discussed earlier, the shape of a protein is critical to its function. For example, an enzyme can bind to a specific substrate at a site known as the active site. If this active site is altered because of local changes or changes in overall protein structure, the enzyme may be unable to bind to the substrate. To understand how the protein gets its final shape or conformation, we need to understand the four levels of protein structure: primary, secondary, tertiary, and quaternary. For a short (4 minutes) introduction video on protein structure click [here](#).

Primary Structure

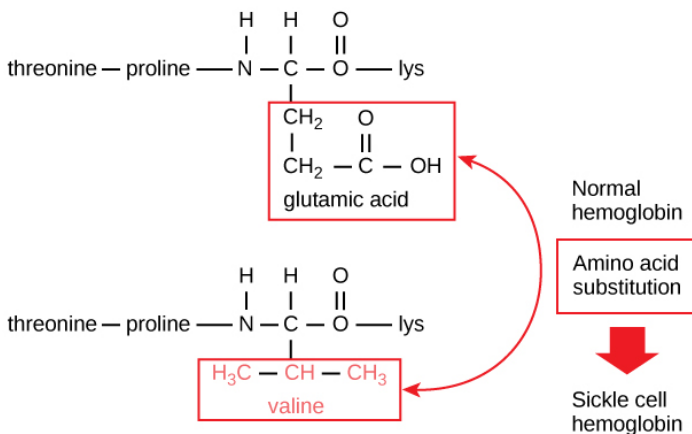
The unique sequence of amino acids in a polypeptide chain is its **primary structure**. For example, the pancreatic hormone insulin has two polypeptide chains, A and B, and they are linked together by disulfide bonds. The N terminal amino acid of the A chain is glycine, whereas the C terminal amino acid is asparagine ([\[link\]](#)). The sequences of amino acids in the A and B chains are unique to insulin.



Bovine serum insulin is a protein hormone made of two peptide chains, A (21 amino acids long) and B (30 amino acids long). In each chain, primary structure is indicated by three-letter abbreviations that represent the names of the amino acids in the order they are present. The amino acid cysteine (cys) has a sulfhydryl (SH) group as a side chain. Two sulfhydryl groups can react in the presence of oxygen to form a disulfide (S-S) bond. Two disulfide bonds connect the A and B chains together, and a third helps the A chain fold into the correct shape. Note that all disulfide bonds are the same length, but are drawn different sizes for clarity.

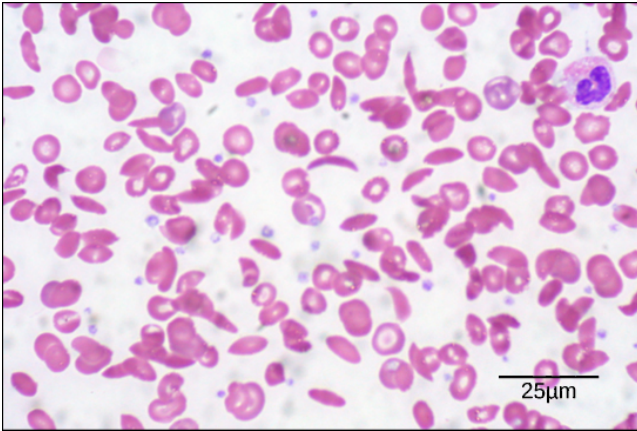
The unique sequence for every protein is ultimately determined by the gene encoding the protein. A change in nucleotide sequence of the gene's coding region may lead to a different amino acid being added to the growing polypeptide chain, causing a change in protein structure and function. In sickle cell anemia, the hemoglobin β chain (a small portion of which is shown in [\[link\]](#)) has a single amino acid substitution, causing a change in protein structure and function. Specifically, the amino acid glutamic acid is substituted by valine in the β chain. What is most remarkable to consider is that a hemoglobin molecule is made up of two alpha chains and two beta

chains that each consist of about 150 amino acids. The molecule, therefore, has about 600 amino acids. The structural difference between a normal hemoglobin molecule and a sickle cell molecule—which dramatically decreases life expectancy—is a single amino acid of the 600. What is even more remarkable is that those 600 amino acids are encoded by three nucleotides each, and the mutation is caused by a single base change (point mutation), 1 in 1800 bases.



The beta chain of hemoglobin is 147 residues in length, yet a single amino acid substitution leads to sickle cell anemia. In normal hemoglobin, the amino acid at position seven is glutamate. In sickle cell hemoglobin, this glutamate is replaced by a valine.

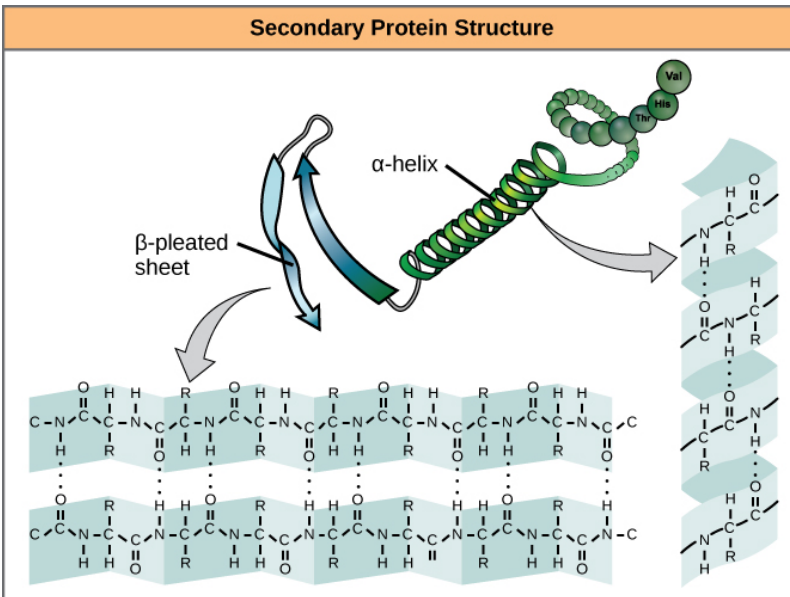
Because of this change of one amino acid in the chain, hemoglobin molecules form long fibers that distort the biconcave, or disc-shaped, red blood cells and assume a crescent or “sickle” shape, which clogs arteries ([link](#)). This can lead to myriad serious health problems such as breathlessness, dizziness, headaches, and abdominal pain for those affected by this disease.



In this blood smear, visualized at 535x magnification using bright field microscopy, sickle cells are crescent shaped, while normal cells are disc-shaped. (credit: modification of work by Ed Uthman; scale-bar data from Matt Russell)

Secondary Structure

The local folding of the polypeptide in some regions gives rise to the **secondary structure** of the protein. The most common are the **α -helix** and **β -pleated sheet** structures ([\[link\]](#)). Both structures are the α -helix structure—the helix held in shape by hydrogen bonds. The hydrogen bonds form between the oxygen atom in the carbonyl group in one amino acid and another amino acid that is four amino acids farther along the chain.

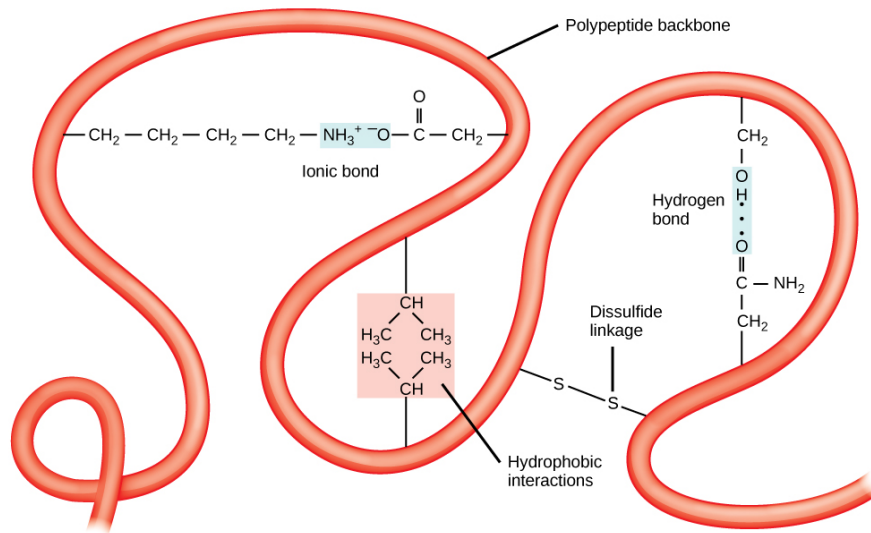


The α -helix and β -pleated sheet are secondary structures of proteins that form because of hydrogen bonding between carbonyl and amino groups in the peptide backbone. Certain amino acids have a propensity to form an α -helix, while others have a propensity to form a β -pleated sheet.

Every helical turn in an alpha helix has 3.6 amino acid residues. The R groups (the variant groups) of the polypeptide protrude out from the α -helix chain. In the β -pleated sheet, the “pleats” are formed by hydrogen bonding between atoms on the backbone of the polypeptide chain. The R groups are attached to the carbons and extend above and below the folds of the pleat. The pleated segments align parallel or antiparallel to each other, and hydrogen bonds form between the partially positive nitrogen atom in the amino group and the partially negative oxygen atom in the carbonyl group of the peptide backbone. The α -helix and β -pleated sheet structures are found in most globular and fibrous proteins and they play an important structural role.

Tertiary Structure

The unique three-dimensional structure of a polypeptide is its **tertiary structure** ([\[link\]](#)). This structure is in part due to chemical interactions at work on the polypeptide chain. Primarily, the interactions among R groups creates the complex three-dimensional tertiary structure of a protein. The nature of the R groups found in the amino acids involved can counteract the formation of the hydrogen bonds described for standard secondary structures. For example, R groups with like charges are repelled by each other and those with unlike charges are attracted to each other (ionic bonds). When protein folding takes place, the hydrophobic R groups of nonpolar amino acids lay in the interior of the protein, whereas the hydrophilic R groups lay on the outside. These types of interactions are also known as hydrophobic interactions. Interaction between cysteine side chains forms disulfide linkages in the presence of oxygen, the only covalent bond forming during protein folding.



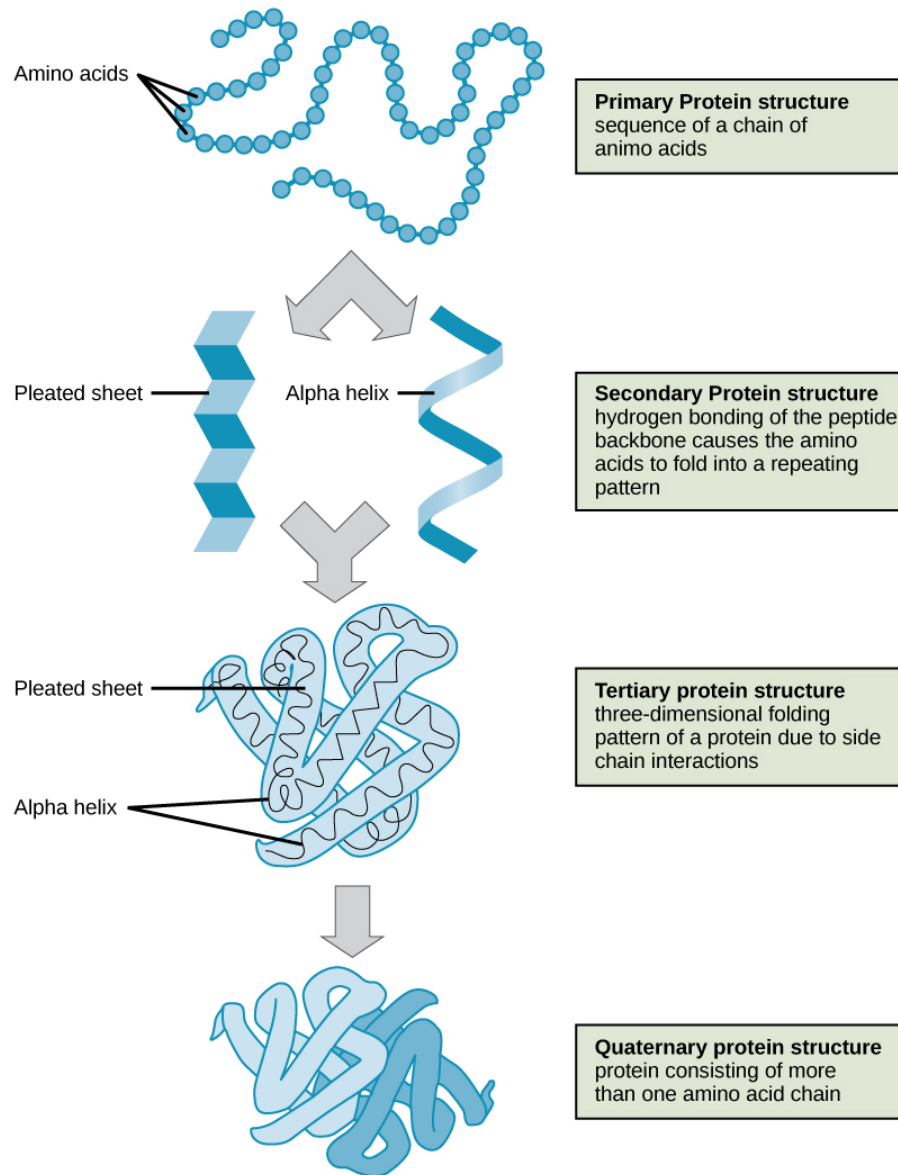
The tertiary structure of proteins is determined by a variety of chemical interactions. These include hydrophobic interactions, ionic bonding, hydrogen bonding and disulfide linkages.

All of these interactions, weak and strong, determine the final three-dimensional shape of the protein. When a protein loses its three-dimensional shape, it may no longer be functional.

Quaternary Structure

In nature, some proteins are formed from several polypeptides, also known as subunits, and the interaction of these subunits forms the **quaternary structure**. Weak interactions between the subunits help to stabilize the overall structure. For example, insulin (a globular protein) has a combination of hydrogen bonds and disulfide bonds that cause it to be mostly clumped into a ball shape. Insulin starts out as a single polypeptide and loses some internal sequences in the presence of post-translational modification after the formation of the disulfide linkages that hold the remaining chains together. Silk (a fibrous protein), however, has a β -pleated sheet structure that is the result of hydrogen bonding between different chains.

The four levels of protein structure (primary, secondary, tertiary, and quaternary) are illustrated in [\[link\]](#).



The four levels of protein structure can be observed in these illustrations. (credit: modification of work by National Human Genome Research Institute)

Denaturation and Protein Folding

Each protein has its own unique sequence and shape that are held together by chemical interactions. If the protein is subject to changes in temperature, pH, or exposure to chemicals, the protein structure may change, losing its shape without losing its primary sequence in what is known as denaturation. Denaturation is often reversible because the primary structure of the polypeptide is conserved in the process if the denaturing agent is removed, allowing the protein to resume its function. Sometimes denaturation is irreversible, leading to loss of function. One example of irreversible protein denaturation is when an egg is fried. The albumin protein in the liquid egg white is denatured when placed in a hot pan. Not all proteins are denatured at high temperatures; for instance, bacteria that survive in hot springs have proteins that function at temperatures close to boiling. The stomach is also very acidic, has a low pH, and denatures proteins as part of the digestion process; however, the digestive enzymes of the stomach retain their activity under these conditions.

Protein folding is critical to its function. It was originally thought that the proteins themselves were responsible for the folding process. Only recently was it found that often they receive assistance in the folding process from protein helpers known as **chaperones** (or chaperonins) that associate with the target protein during the folding process. They act by preventing aggregation of polypeptides that make up the complete protein structure, and they disassociate from the protein once the target protein is folded.

Note:

Link to Learning



For an additional perspective on proteins, view [this animation](#) called “Biomolecules: The Proteins.”

Khan Academy link

[Protein structure.](#)

Exercise:

Problem: Which of the following changes when a protein denatures?

- a. amino acid sequence
- b. length of the entire protein
- c. three dimensional structure
- d. the peptide bonds between the amino acids
- e. a and d
- f. b and d

Solution:

c

Section Summary

Proteins are a class of macromolecules that perform a diverse range of functions for the cell. They help in metabolism by providing structural support and by acting as enzymes, carriers, or hormones. The building blocks of proteins (monomers) are amino acids. Each amino acid has a central carbon that is linked to an amino group, a carboxyl group, a hydrogen atom, and an R group or side chain. There are 20 commonly occurring amino acids, each of which differs in the R group. Each amino acid is linked to its neighbors by a peptide bond. A long chain of amino acids is known as a polypeptide.

Proteins are organized at four levels: primary, secondary, tertiary, and (optional) quaternary. The primary structure is the unique sequence of amino acids. The local folding of the polypeptide to form structures such as the α helix and β -pleated sheet constitutes the secondary structure. The overall three-dimensional structure is the tertiary structure. When two or more polypeptides combine to form the complete protein structure, the configuration is known as the quaternary structure of a protein. Protein

shape and function are intricately linked; any change in shape caused by changes in temperature or pH may lead to protein denaturation and a loss in function.

Art Connections

Exercise:

Problem:

[\[link\]](#) Which categories of amino acid would you expect to find on the surface of a soluble protein, and which would you expect to find in the interior? What distribution of amino acids would you expect to find in a protein embedded in a lipid bilayer?

Solution:

[\[link\]](#) Polar and charged amino acid residues (the remainder after peptide bond formation) are more likely to be found on the surface of soluble proteins where they can interact with water, and nonpolar (e.g., amino acid side chains) are more likely to be found in the interior where they are sequestered from water. In membrane proteins, nonpolar and hydrophobic amino acid side chains associate with the hydrophobic tails of phospholipids, while polar and charged amino acid side chains interact with the polar head groups or with the aqueous solution. However, there are exceptions. Sometimes, positively and negatively charged amino acid side chains interact with one another in the interior of a protein, and polar or charged amino acid side chains that interact with a ligand can be found in the ligand binding pocket.

Review Questions

Exercise:

Problem: The monomers that make up proteins are called _____.

- a. nucleotides
 - b. disaccharides
 - c. amino acids
 - d. chaperones
-

Solution:

C

Exercise:

Problem:

The α helix and the β -pleated sheet are part of which protein structure?

- a. primary
 - b. secondary
 - c. tertiary
 - d. quaternary
-

Solution:

B

Free Response

Exercise:

Problem:

Explain what happens if even one amino acid is substituted for another in a polypeptide chain. Provide a specific example.

Solution:

A change in gene sequence can lead to a different amino acid being added to a polypeptide chain instead of the normal one. This causes a

change in protein structure and function. For example, in sickle cell anemia, the hemoglobin β chain has a single amino acid substitution—the amino acid glutamic acid in position six is substituted by valine. Because of this change, hemoglobin molecules form aggregates, and the disc-shaped red blood cells assume a crescent shape, which results in serious health problems.

Exercise:

Problem: Describe the differences in the four protein structures.

Solution:

The sequence and number of amino acids in a polypeptide chain is its primary structure. The local folding of the polypeptide in some regions is the secondary structure of the protein. The three-dimensional structure of a polypeptide is known as its tertiary structure, created in part by chemical interactions such as hydrogen bonds between polar side chains, van der Waals interactions, disulfide linkages, and hydrophobic interactions. Some proteins are formed from multiple polypeptides, also known as subunits, and the interaction of these subunits forms the quaternary structure.

Glossary

alpha-helix structure (α -helix)

type of secondary structure of proteins formed by folding of the polypeptide into a helix shape with hydrogen bonds stabilizing the structure

amino acid

monomer of a protein; has a central carbon or alpha carbon to which an amino group, a carboxyl group, a hydrogen, and an R group or side chain is attached; the R group is different for all 20 amino acids

beta-pleated sheet (β -pleated)

secondary structure found in proteins in which “pleats” are formed by hydrogen bonding between atoms on the backbone of the polypeptide chain

chaperone

(also, chaperonin) protein that helps nascent protein in the folding process

denaturation

loss of shape in a protein as a result of changes in temperature, pH, or exposure to chemicals

enzyme

catalyst in a biochemical reaction that is usually a complex or conjugated protein

hormone

chemical signaling molecule, usually protein or steroid, secreted by endocrine cells that act to control or regulate specific physiological processes

peptide bond

bond formed between two amino acids by a dehydration reaction

polypeptide

long chain of amino acids linked by peptide bonds

primary structure

linear sequence of amino acids in a protein

protein

biological macromolecule composed of one or more chains of amino acids

quaternary structure

association of discrete polypeptide subunits in a protein

secondary structure

regular structure formed by proteins by intramolecular hydrogen bonding between the oxygen atom of one amino acid residue and the hydrogen attached to the nitrogen atom of another amino acid residue

tertiary structure

three-dimensional conformation of a protein, including interactions between secondary structural elements; formed from interactions between amino acid side chains

Bis2A 03.2 Carbohydrates v1.2

By the end of this section, you will be able to:

- Discuss the role of carbohydrates in cells and in the extracellular materials of animals and plants
- Explain the classifications of carbohydrates
- List common monosaccharides, disaccharides, and polysaccharides

CARBOHYDRATES

Most people are familiar with carbohydrates, one type of macromolecule, especially when it comes to what we eat. To lose weight, some individuals adhere to “low-carb” diets. Athletes, in contrast, often “carb-load” before important competitions to ensure that they have enough energy to compete at a high level. Carbohydrates are, in fact, an essential part of our diet; grains, fruits, and vegetables are all natural sources of carbohydrates. Carbohydrates provide energy to the body, particularly through glucose, a simple sugar that is a component of **starch** and an ingredient in many staple foods. Carbohydrates also have other important functions in humans, animals, and plants.

Molecular Structures

Carbohydrates can be represented by the stoichiometric formula $(\text{CH}_2\text{O})_n$, where n is the number of carbons in the molecule. In other words, the ratio of carbon to hydrogen to oxygen is 1:2:1 in carbohydrate molecules. This formula also explains the origin of the term “carbohydrate”: the components are carbon (“carbo”) and the components of water (hence, “hydrate”). Carbohydrates are classified into three subtypes: monosaccharides, disaccharides, and polysaccharides.

Nomenclature

One issue with carbohydrate chemistry is the nomenclature. Here are a few quick and simple rules:

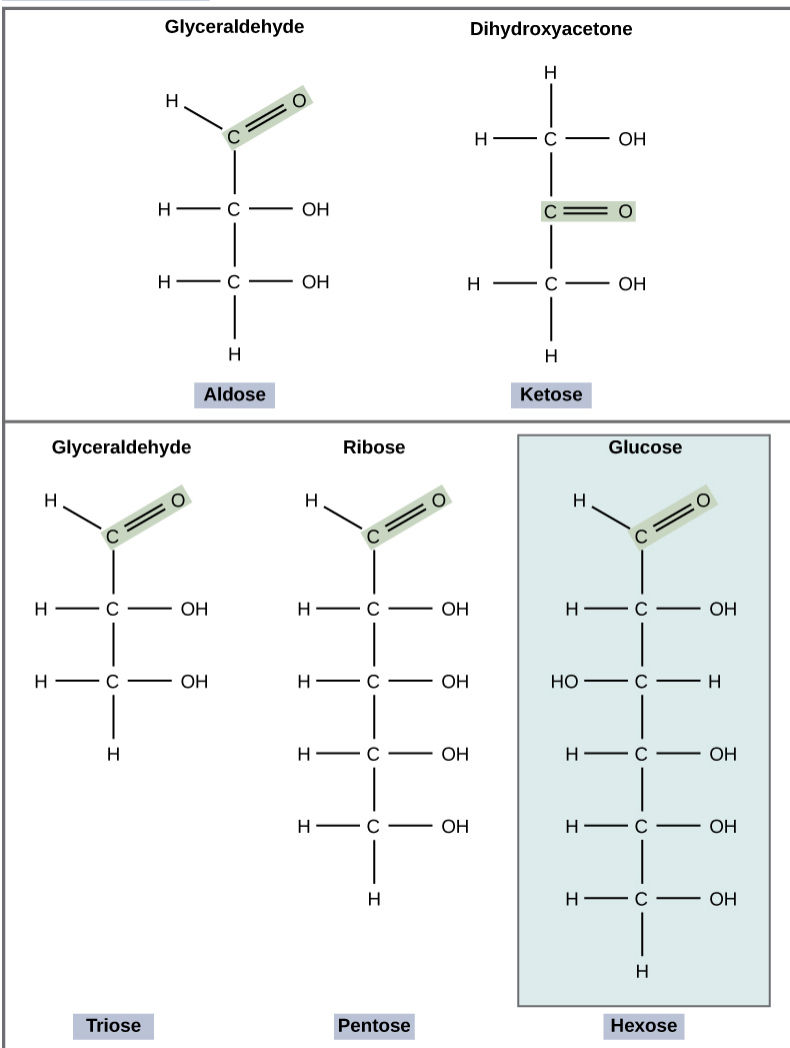
1. Simple carbohydrates end with an "...ose"; such as glucose, lactose, or dexrose
2. Simple carbohydrates can be classified based on the number of carbon atoms in the sugar, such as a triose (3-carbons), pentose (5-carbons) or hexose (6-carbons).
3. Simple Carbohydrates can be classified based on the functional group found in the molecule, such as either a ketoses or aldoses
4. Polysaccharides are often organized by the number of sugar molecules in the chain, such as a monosaccharide, disaccharide or trisaccharide.

These will be explained in detail below. For a short video on carbohydrate classification see the Khan academy video (10 minutes in length) by clicking [here](#).

Monosaccharides

Monosaccharides (mono- = “one”; sacchar- = “sweet”) are simple sugars, the most common of which is glucose. In monosaccharides, the number of carbons usually ranges from three to seven. Most monosaccharide names end with the suffix -ose. If the sugar has an aldehyde group (the functional group with the structure $R-CHO$), it is known as an aldose, and if it has a ketone group (the functional group with the structure $RC(=O)R'$), it is known as a ketose. Depending on the number of carbons in the sugar, they also may be known as trioses (three carbons), pentoses (five carbons), and or hexoses (six carbons). See [\[link\]](#) for an illustration of the monosaccharides.

MONOSACCHARIDES



Monosaccharides are classified based on the position of their carbonyl group and the number of carbons in the backbone. Aldoses have a carbonyl group (indicated in green) at the end of the carbon chain, and ketoses have a carbonyl group in the middle of the carbon chain. Trioses, pentoses, and hexoses have three, five, and six carbon backbones, respectively.

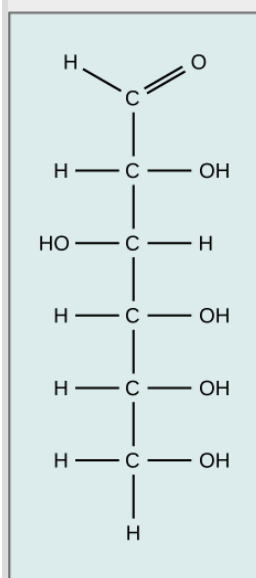
The chemical formula for glucose is $C_6H_{12}O_6$. In humans, glucose is an important source of energy. During cellular respiration, energy is released from glucose, and that energy is used to help make adenosine triphosphate (ATP). Plants synthesize glucose using carbon dioxide and water, and glucose in turn is used for energy requirements for the plant. Excess glucose is often stored as starch that is catabolized (the breakdown of larger molecules by cells) by humans and other animals that feed on plants.

Galactose (part of lactose, or milk sugar) and fructose (found in sucrose, in fruit) are other common monosaccharides. Although glucose, galactose, and fructose all have the same chemical formula ($C_6H_{12}O_6$), they differ structurally and chemically (and are known as isomers) because of the different arrangement of functional groups around the asymmetric carbon; all of these monosaccharides have more than one asymmetric carbon ([link](#)).

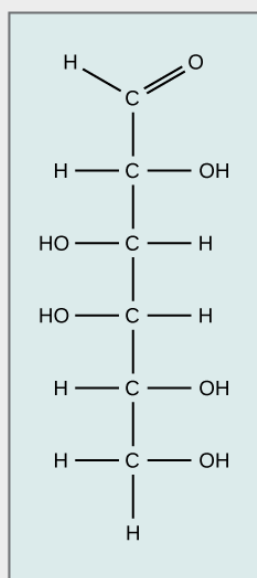
Note:

Art Connection

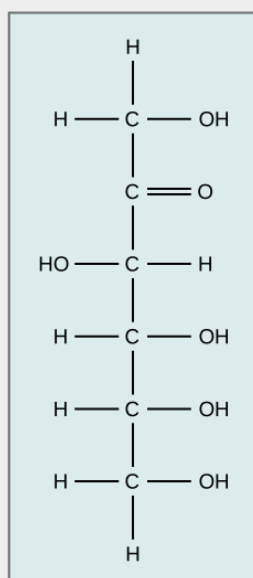
Glucose



Galactose



Fructose



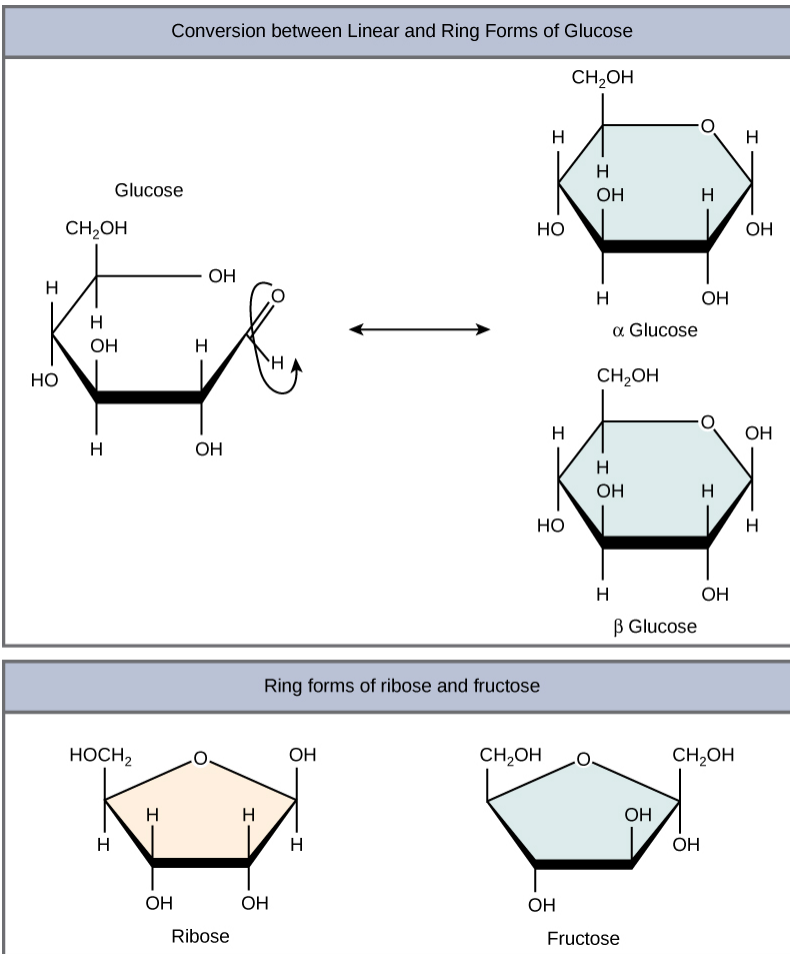
Glucose, galactose, and fructose are all hexoses. They are structural isomers, meaning they have the same chemical

formula ($C_6H_{12}O_6$) but a different arrangement of atoms.

What kind of sugars are these, aldose or ketose?

Glucose, galactose, and fructose are isomeric monosaccharides (hexoses), meaning they have the same chemical formula but have slightly different structures. Glucose and galactose are aldoses, and fructose is a ketose.

Monosaccharides can exist as a linear chain or as ring-shaped molecules; in aqueous solutions they are usually found in ring forms ([link](#)). Glucose in a ring form can have two different arrangements of the hydroxyl group (OH) around the anomeric carbon (carbon 1 that becomes asymmetric in the process of ring formation). If the hydroxyl group is below carbon number 1 in the sugar, it is said to be in the alpha (α) position, and if it is above the plane, it is said to be in the beta (β) position.

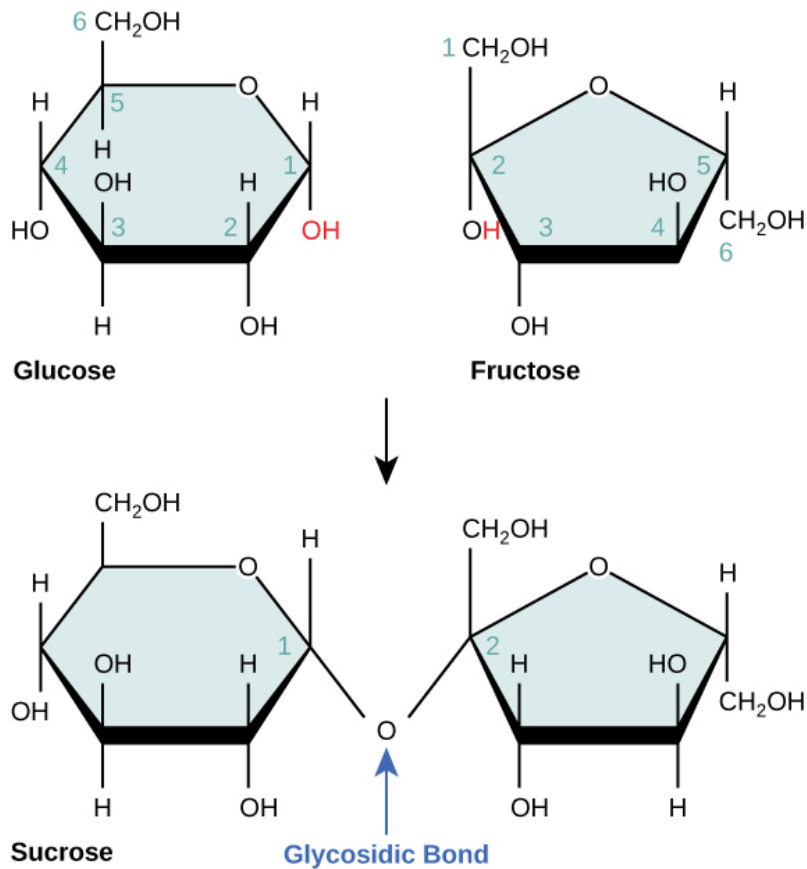


Five and six carbon monosaccharides exist in equilibrium between linear and ring forms. When the ring forms, the side chain it closes on is locked into an α or β position.

Fructose and ribose also form rings, although they form five-membered rings as opposed to the six-membered ring of glucose.

Disaccharides

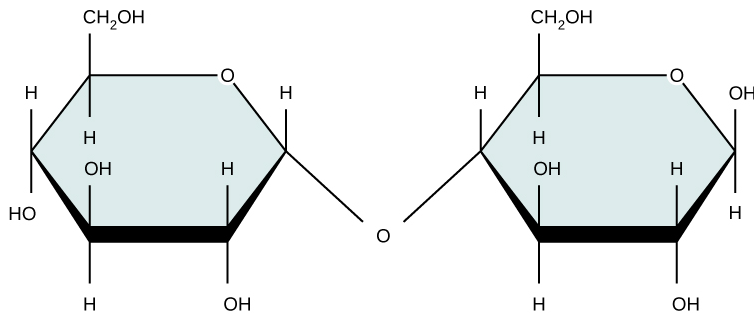
Disaccharides (di- = “two”) form when two monosaccharides undergo a dehydration reaction (also known as a condensation reaction or dehydration synthesis). During this process, the hydroxyl group of one monosaccharide combines with the hydrogen of another monosaccharide, releasing a molecule of water and forming a covalent bond. A covalent bond formed between a carbohydrate molecule and another molecule (in this case, between two monosaccharides) is known as a **glycosidic bond** ([\[link\]](#)). Glycosidic bonds (also called glycosidic linkages) can be of the alpha or the beta type.



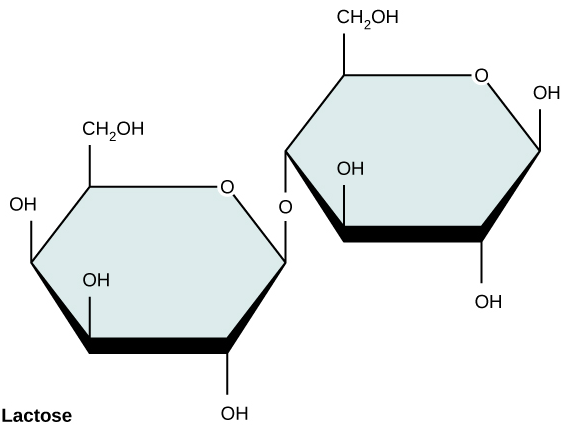
Sucrose is formed when a monomer of glucose and a monomer of fructose are joined in a dehydration reaction to form a glycosidic bond. In the process, a water molecule is lost. By convention, the carbon

atoms in a monosaccharide are numbered from the terminal carbon closest to the carbonyl group. In sucrose, a glycosidic linkage is formed between carbon 1 in glucose and carbon 2 in fructose.

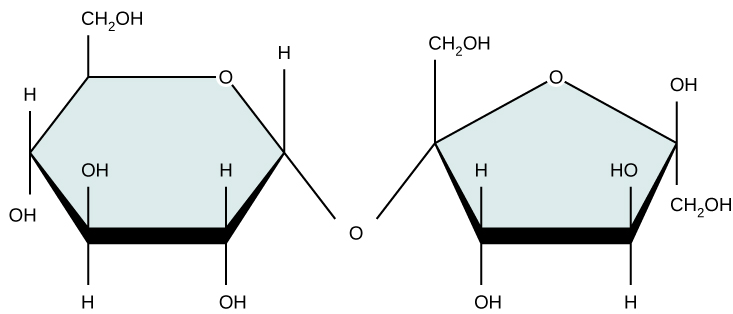
Common disaccharides include lactose, maltose, and sucrose ([\[link\]](#)). Lactose is a disaccharide consisting of the monomers glucose and galactose. It is found naturally in milk. Maltose, or malt sugar, is a disaccharide formed by a dehydration reaction between two glucose molecules. The most common disaccharide is sucrose, or table sugar, which is composed of the monomers glucose and fructose.



Maltose



Lactose



Sucrose

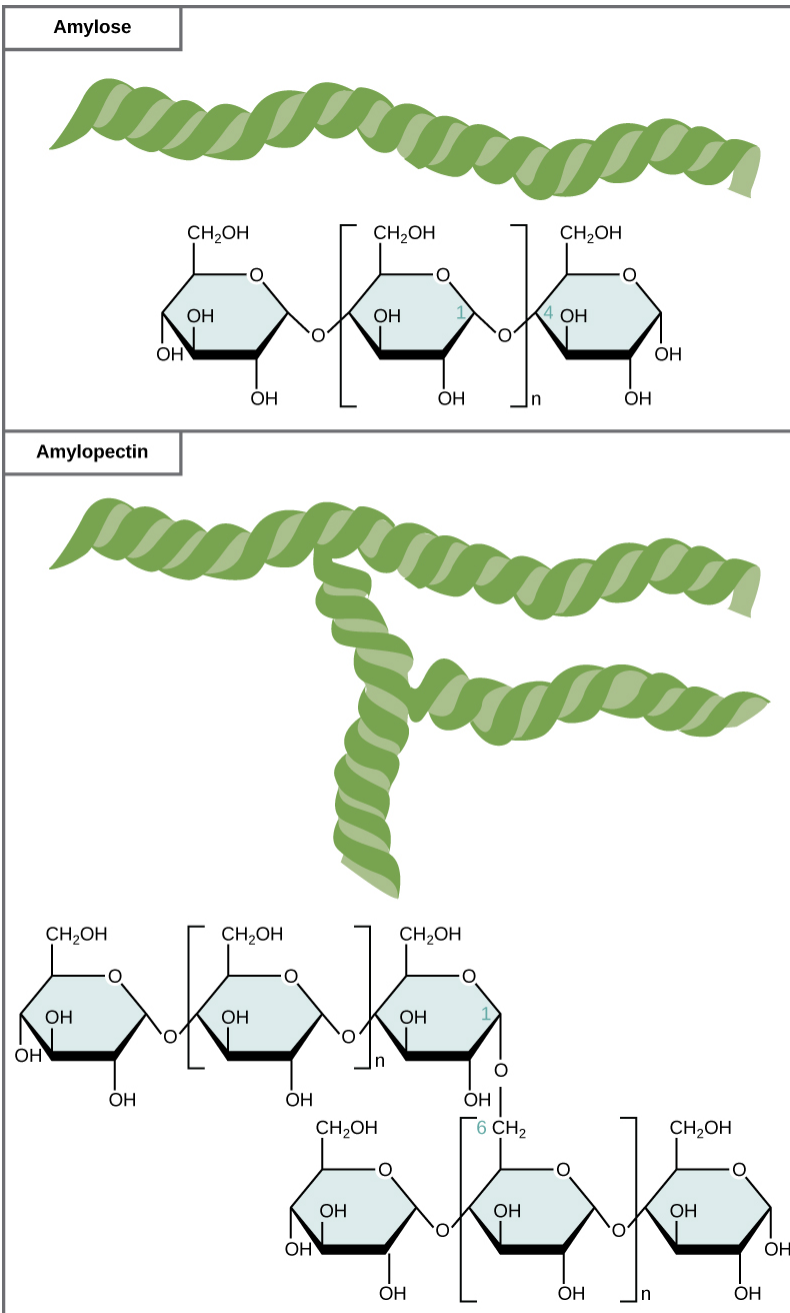
Common disaccharides include maltose (grain sugar), lactose (milk sugar), and sucrose (table sugar).

Polysaccharides

A long chain of monosaccharides linked by glycosidic bonds is known as a **polysaccharide** (poly- = “many”). The chain may be branched or unbranched, and it may contain different types of monosaccharides. The molecular weight may be 100,000 daltons or more depending on the number of monomers joined. Starch, glycogen, cellulose, and chitin are primary examples of polysaccharides.

Starch is the stored form of sugars in plants and is made up of a mixture of amylose and amylopectin (both polymers of glucose). Plants are able to synthesize glucose, and the excess glucose, beyond the plant’s immediate energy needs, is stored as starch in different plant parts, including roots and seeds. The starch in the seeds provides food for the embryo as it germinates and can also act as a source of food for humans and animals. The starch that is consumed by humans is broken down by enzymes, such as salivary amylases, into smaller molecules, such as maltose and glucose. The cells can then absorb the glucose.

Starch is made up of glucose monomers that are joined by α 1-4 or α 1-6 glycosidic bonds. The numbers 1-4 and 1-6 refer to the carbon number of the two residues that have joined to form the bond. As illustrated in [\[link\]](#), amylose is starch formed by unbranched chains of glucose monomers (only α 1-4 linkages), whereas amylopectin is a branched polysaccharide (α 1-6 linkages at the branch points).



Amylose and amylopectin are two different forms of starch. Amylose is composed of unbranched chains of glucose monomers connected by α 1,4 glycosidic linkages.

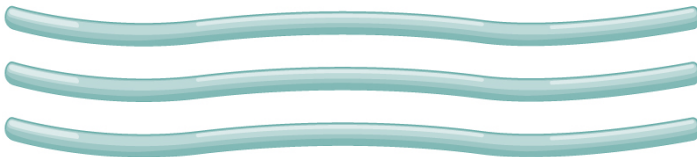
Amylopectin is composed of branched chains of glucose monomers connected by α 1,4 and α 1,6 glycosidic linkages. Because

of the way the subunits are joined, the glucose chains have a helical structure. Glycogen (not shown) is similar in structure to amylopectin but more highly branched.

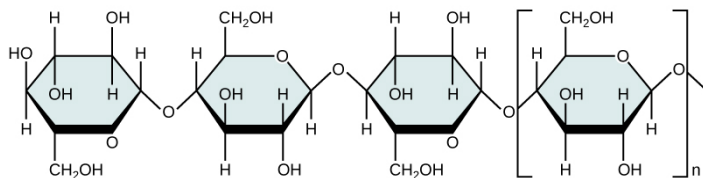
Glycogen is the storage form of glucose in humans and other vertebrates and is made up of monomers of glucose. Glycogen is the animal equivalent of starch and is a highly branched molecule usually stored in liver and muscle cells. Whenever blood glucose levels decrease, glycogen is broken down to release glucose in a process known as glycogenolysis.

Cellulose is the most abundant natural biopolymer. The cell wall of plants is mostly made of cellulose; this provides structural support to the cell. Wood and paper are mostly cellulosic in nature. Cellulose is made up of glucose monomers that are linked by β 1-4 glycosidic bonds ([\[link\]](#)).

Cellulose fibers



Cellulose structure



In cellulose, glucose monomers are linked in unbranched chains by β 1-4 glycosidic linkages. Because of the way the glucose subunits are joined, every glucose monomer is flipped relative to the next one resulting in a linear, fibrous structure.

As shown in [\[link\]](#), every other glucose monomer in cellulose is flipped over, and the monomers are packed tightly as extended long chains. This gives cellulose its rigidity and high tensile strength—which is so important to plant cells. While the β 1-4 linkage cannot be broken down by human digestive enzymes, herbivores such as cows, koalas, buffalos, and horses are able, with the help of the specialized flora in their stomach, to digest plant material that is rich in cellulose and use it as a food source. In these animals, certain species of bacteria and protists reside in the rumen (part of the digestive system of herbivores) and secrete the enzyme cellulase. The appendix of grazing animals also contains bacteria that digest cellulose, giving it an important role in the digestive systems of ruminants. Cellulases can break down cellulose into glucose monomers that can be used as an energy source by the animal. Termites are also able to break down cellulose because of the presence of other organisms in their bodies that secrete cellulases.

Carbohydrates serve various functions in different animals. Arthropods (insects, crustaceans, and others) have an outer skeleton, called the exoskeleton, which protects their internal body parts (as seen in the bee in [\[link\]](#)). This exoskeleton is made of the biological macromolecule **chitin**, which is a polysaccharide-containing nitrogen. It is made of repeating units of N-acetyl- β -d-glucosamine, a modified sugar. Chitin is also a major component of fungal cell walls; fungi are neither animals nor plants and form a kingdom of their own in the domain Eukarya.



Insects have a hard outer exoskeleton made of chitin, a type of polysaccharide. (credit: Louise Docker)

Exercise:

Problem: Which of the following is a characteristic of carbohydrates?

- a. Carbohydrates are hydrophobic and have the general formula CH_2O
- b. Carbohydrates are hydrophobic and have the general formula CHO
- c. Carbohydrates are hydrophilic and have the general formula CHO
- d. Carbohydrates are hydrophilic and have the general formula CH_2O

Solution:

D

Benefits of Carbohydrates

Are carbohydrates good for you? People who wish to lose weight are often told that carbohydrates are bad for them and should be avoided. Some diets completely forbid carbohydrate consumption, claiming that a low-carbohydrate diet helps people to lose weight faster. However, carbohydrates have been an important part of the human diet for thousands of years; artifacts from ancient civilizations show the presence of wheat, rice, and corn in our ancestors' storage areas.

Carbohydrates should be supplemented with proteins, vitamins, and fats to be parts of a well-balanced diet. Calorie-wise, a gram of carbohydrate provides 4.3 Kcal. For comparison, fats provide 9 Kcal/g, a less desirable ratio. Carbohydrates contain soluble and insoluble elements; the insoluble part is known as fiber, which is mostly cellulose. Fiber has many uses; it promotes regular bowel movement by adding bulk, and it regulates the rate of consumption of blood glucose. Fiber also helps to remove excess cholesterol from the body: fiber binds to the cholesterol in the small intestine, then attaches to the cholesterol and prevents the cholesterol particles from entering the bloodstream, and then cholesterol exits the body via the feces. Fiber-rich diets also have a protective role in reducing the occurrence of colon cancer. In addition, a meal containing whole grains and vegetables gives a feeling of fullness. As an immediate source of energy, glucose is broken down during the process of cellular respiration, which produces ATP, the energy currency of the cell. Without the consumption of carbohydrates, the availability of “instant energy” would be reduced. Eliminating carbohydrates from the diet is not the best way to lose weight. A low-calorie diet that is rich in whole grains, fruits, vegetables, and lean meat, together with plenty of exercise and plenty of water, is the more sensible way to lose weight.

Note:

[Link to Learning](#)



For an additional perspective on carbohydrates, explore “Biomolecules: the Carbohydrates” through this [interactive animation](#).

For a more details on carbohydrates go to UC Davis Chemwiki pages on Carbohydrates at [Chemwiki Carbohydrates](#)

Exercise:

Problem: Which of the following are functions of carbohydrates?

- a. energy storage
- b. structure
- c. cell recognition
- d. cell signaling
- e. a, b and c
- f. all of the above

Solution:

f

Section Summary

Carbohydrates are a group of macromolecules that are a vital energy source for the cell and provide structural support to plant cells, fungi, and all of the arthropods that include lobsters, crabs, shrimp, insects, and spiders.

Carbohydrates are classified as monosaccharides, disaccharides, and polysaccharides depending on the number of monomers in the molecule.

Monosaccharides are linked by glycosidic bonds that are formed as a result of dehydration reactions, forming disaccharides and polysaccharides with the elimination of a water molecule for each bond formed. Glucose, galactose, and fructose are common monosaccharides, whereas common disaccharides include lactose, maltose, and sucrose. Starch and glycogen, examples of polysaccharides, are the storage forms of glucose in plants and animals, respectively. The long polysaccharide chains may be branched or unbranched. Cellulose is an example of an unbranched polysaccharide, whereas amylopectin, a constituent of starch, is a highly branched molecule. Storage of glucose, in the form of polymers like starch or glycogen, makes it slightly less accessible for metabolism; however, this prevents it from leaking out of the cell or creating a high osmotic pressure that could cause excessive water uptake by the cell.

Art Connections

Exercise:

Problem: [\[link\]](#) What kind of sugars are these, aldose or ketose?

Solution:

[\[link\]](#) Glucose and galactose are aldoses. Fructose is a ketose.

Review Questions

Exercise:

Problem: An example of a monosaccharide is _____.

- a. fructose
- b. glucose
- c. galactose
- d. all of the above

Solution:

D

Exercise:

Problem: Cellulose and starch are examples of:

- a. monosaccharides
- b. disaccharides
- c. lipids
- d. polysaccharides

Solution:

D

Exercise:

Problem:

Plant cell walls contain which of the following in abundance?

- a. starch
- b. cellulose
- c. glycogen
- d. lactose

Solution:

B

Exercise:

Problem:

Lactose is a disaccharide formed by the formation of a _____ bond between glucose and _____.

- a. glycosidic; lactose
 - b. glycosidic; galactose
 - c. hydrogen; sucrose
 - d. hydrogen; fructose
-

Solution:

B

Free Response

Exercise:

Problem:

Describe the similarities and differences between glycogen and starch.

Solution:

Glycogen and starch are polysaccharides. They are the storage form of glucose. Glycogen is stored in animals in the liver and in muscle cells, whereas starch is stored in the roots, seeds, and leaves of plants. Starch has two different forms, one unbranched (amylose) and one branched (amylopectin), whereas glycogen is a single type of a highly branched molecule.

Exercise:

Problem:

Why is it impossible for humans to digest food that contains cellulose?

Solution:

The β 1-4 glycosidic linkage in cellulose cannot be broken down by human digestive enzymes. Herbivores such as cows, buffalos, and horses are able to digest grass that is rich in cellulose and use it as a food source because bacteria and protists in their digestive systems,

especially in the rumen, secrete the enzyme cellulase. Cellulases can break down cellulose into glucose monomers that can be used as an energy source by the animal.

Glossary

carbohydrate

biological macromolecule in which the ratio of carbon to hydrogen and to oxygen is 1:2:1; carbohydrates serve as energy sources and structural support in cells and form the a cellular exoskeleton of arthropods

cellulose

polysaccharide that makes up the cell wall of plants; provides structural support to the cell

chitin

type of carbohydrate that forms the outer skeleton of all arthropods that include crustaceans and insects; it also forms the cell walls of fungi

disaccharide

two sugar monomers that are linked together by a glycosidic bond

glycogen

storage carbohydrate in animals

glycosidic bond

bond formed by a dehydration reaction between two monosaccharides with the elimination of a water molecule

monosaccharide

single unit or monomer of carbohydrates

polysaccharide

long chain of monosaccharides; may be branched or unbranched

starch

storage carbohydrate in plants

Bis2A 03.3 Lipids v1.2

By the end of this section, you will be able to:

- Describe the four major types of lipids
- Explain the role of fats in storing energy
- Differentiate between saturated and unsaturated fatty acids
- Describe phospholipids and their role in cells
- Define the basic structure of a steroid and some functions of steroids
- Explain the how cholesterol helps to maintain the fluid nature of the plasma membrane

Lipids include a diverse group of compounds that are largely nonpolar in nature. This is because they are hydrocarbons that include mostly nonpolar carbon–carbon or carbon–hydrogen bonds. Non-polar molecules are hydrophobic (“water fearing”), or insoluble in water. Lipids perform many different functions in a cell. Cells store energy for long-term use in the form of fats. Lipids also provide insulation from the environment for plants and animals ([\[link\]](#)). For example, they help keep aquatic birds and mammals dry when forming a protective layer over fur or feathers because of their water-repellant hydrophobic nature. Lipids are also the building blocks of many hormones and are an important constituent of all cellular membranes. Lipids include fats, oils, waxes, phospholipids, and steroids.



Hydrophobic lipids in the fur
of aquatic mammals, such as

this river otter, protect them
from the elements. (credit:
Ken Bosma)

Fats and Oils

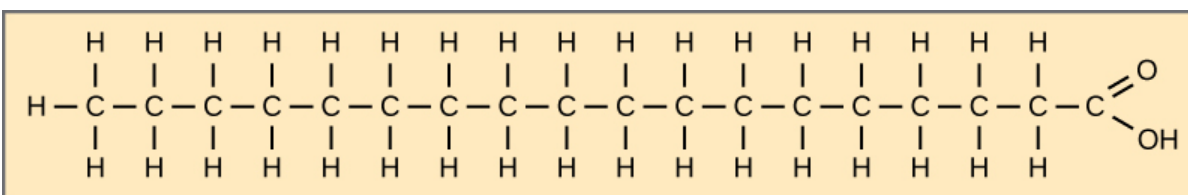
A fat molecule consists of two main components—glycerol and fatty acids. Glycerol is an organic compound (alcohol) with three carbons, five hydrogens, and three hydroxyl (OH) groups. Fatty acids have a long chain of hydrocarbons to which a carboxyl group is attached, hence the name “fatty acid.” The number of carbons in the fatty acid may range from 4 to 36; most common are those containing 12–18 carbons. In a fat molecule, the fatty acids are attached to each of the three carbons of the glycerol molecule with an ester bond through an oxygen atom ([\[link\]](#)).

$$\begin{array}{c} \text{H} \\ | \\ \text{H}-\text{C}-\text{OH} \\ | \\ \text{H}-\text{C}-\text{OH} \\ | \\ \text{H}-\text{C}-\text{OH} \\ | \\ \text{H} \end{array}$$
CCCCCCCCCCCCCCCCO

During this ester bond formation, three water molecules are released. The three fatty acids in the triacylglycerol may be similar or dissimilar. Fats are also called **triacylglycerols** or **triglycerides** because of their chemical

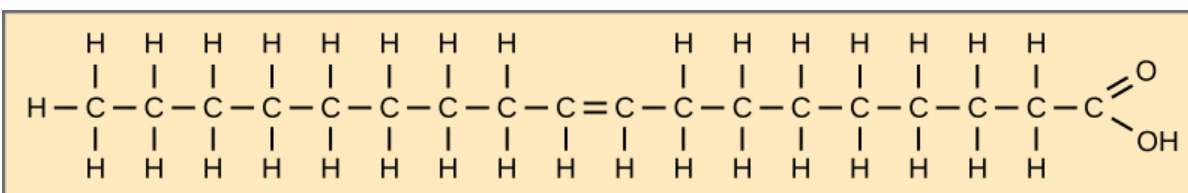
structure. Some fatty acids have common names that specify their origin. For example, palmitic acid, a **saturated fatty acid**, is derived from the palm tree. Arachidic acid is derived from *Arachis hypogea*, the scientific name for groundnuts or peanuts.

Fatty acids may be saturated or unsaturated. In a fatty acid chain, if there are only single bonds between neighboring carbons in the hydrocarbon chain, the fatty acid is said to be saturated. Saturated fatty acids are saturated with hydrogen; in other words, the number of hydrogen atoms attached to the carbon skeleton is maximized. Stearic acid is an example of a saturated fatty acid ([\[link\]](#))



Stearic acid is a common saturated fatty acid.

When the hydrocarbon chain contains a double bond, the fatty acid is said to be **unsaturated**. Oleic acid is an example of an unsaturated fatty acid ([\[link\]](#)).



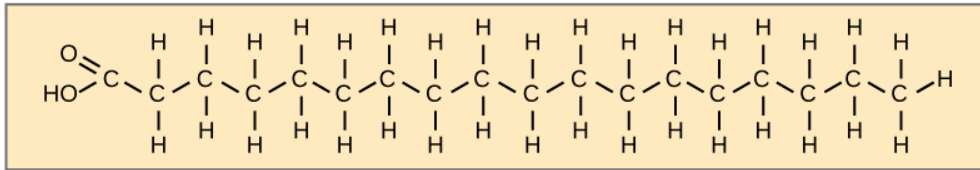
Oleic acid is a common unsaturated fatty acid.

Most unsaturated fats are liquid at room temperature and are called oils. If there is one double bond in the molecule, then it is known as a monounsaturated fat (e.g., olive oil), and if there is more than one double bond, then it is known as a polyunsaturated fat (e.g., canola oil).

When a fatty acid has no double bonds, it is known as a saturated fatty acid because no more hydrogen may be added to the carbon atoms of the chain. A fat may contain similar or different fatty acids attached to glycerol. Long straight fatty acids with single bonds tend to get packed tightly and are solid at room temperature. Animal fats with stearic acid and palmitic acid (common in meat) and the fat with butyric acid (common in butter) are examples of saturated fats. Mammals store fats in specialized cells called adipocytes, where globules of fat occupy most of the cell's volume. In plants, fat or oil is stored in many seeds and is used as a source of energy during seedling development. Unsaturated fats or oils are usually of plant origin and contain *cis* unsaturated fatty acids. *Cis* and *trans* indicate the configuration of the molecule around the double bond. If hydrogens are present in the same plane, it is referred to as a *cis* fat; if the hydrogen atoms are on two different planes, it is referred to as a **trans fat**. The *cis* double bond causes a bend or a “kink” that prevents the fatty acids from packing tightly, keeping them liquid at room temperature ([\[link\]](#)). Olive oil, corn oil, canola oil, and cod liver oil are examples of unsaturated fats. Unsaturated fats help to lower blood cholesterol levels whereas saturated fats contribute to plaque formation in the arteries.

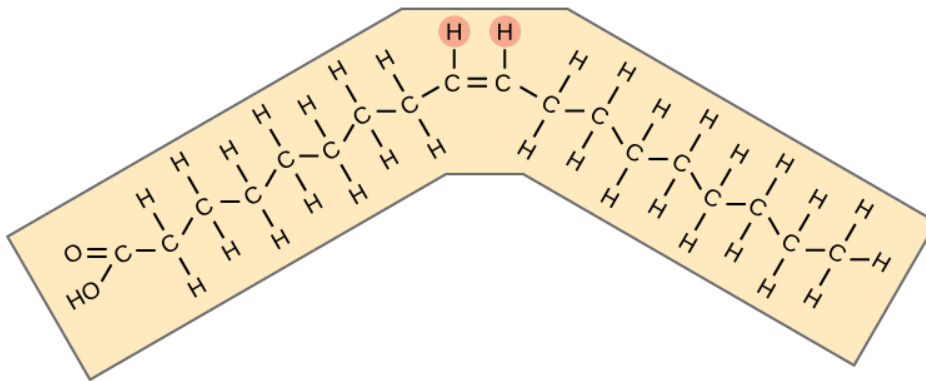
Saturated fatty acid

Stearic acid

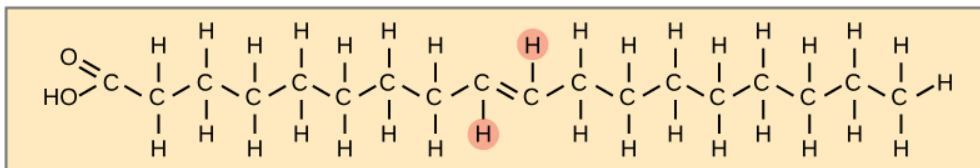


Unsaturated fatty acids

Cis oleic acid



Trans oleic acid



Saturated fatty acids have hydrocarbon chains connected by single bonds only. Unsaturated fatty acids have one or more double bonds. Each double bond may be in a *cis* or *trans* configuration. In the *cis* configuration, both hydrogens are on the same side of the hydrocarbon chain. In the *trans* configuration, the hydrogens are on opposite sides. A *cis* double bond causes a kink in the chain.

Trans Fats

In the food industry, oils are artificially hydrogenated to make them semi-solid and of a consistency desirable for many processed food products. Simply speaking, hydrogen gas is bubbled through oils to solidify them. During this hydrogenation process, double bonds of the *cis*- conformation in the hydrocarbon chain may be converted to double bonds in the *trans*-conformation.

Margarine, some types of peanut butter, and shortening are examples of artificially hydrogenated *trans* fats. Recent studies have shown that an increase in *trans* fats in the human diet may lead to an increase in levels of low-density lipoproteins (LDL), or “bad” cholesterol, which in turn may lead to plaque deposition in the arteries, resulting in heart disease. Many fast food restaurants have recently banned the use of *trans* fats, and food labels are required to display the *trans* fat content.

Exercise:

Problem: *Trans* fats occur when:

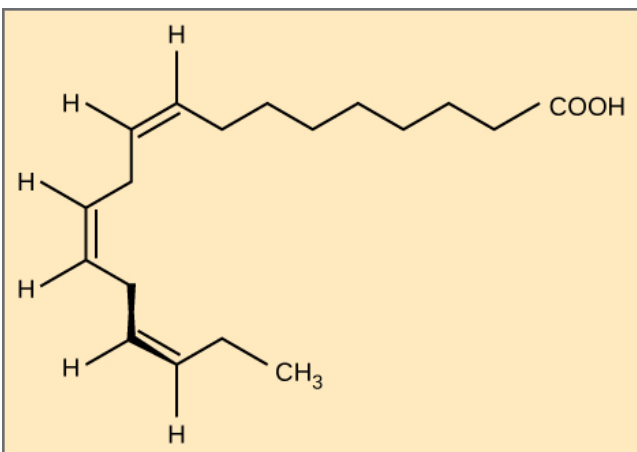
- a. saturated fatty acids are hydrogenated in the lab to produce unsaturated fatty acids
- b. plants produce saturated fatty acids
- c. unsaturated fatty acids are hydrogenated in the lab to produce saturated fatty acids
- d. animals produce unsaturated fatty acids
- e. a and c
- f. b and d

Solution:

Insert Solution Text Here

Omega Fatty Acids

Essential fatty acids are fatty acids required but not synthesized by the human body. Consequently, they have to be supplemented through ingestion via the diet. **Omega-3** fatty acids (like that shown in [\[link\]](#)) fall into this category and are one of only two known for humans (the other being omega-6 fatty acid). These are polyunsaturated fatty acids and are called omega-3 because the third carbon from the end of the hydrocarbon chain is connected to its neighboring carbon by a double bond.



Alpha-linolenic acid is an example of an omega-3 fatty acid. It has three *cis* double bonds and, as a result, a curved shape. For clarity, the carbons are not shown. Each singly bonded carbon has two hydrogens associated with it, also not shown.

The farthest carbon away from the carboxyl group is numbered as the omega (ω) carbon, and if the double bond is between the third and fourth carbon from that end, it is known as an omega-3 fatty acid. Nutritionally important because the body does not make them, omega-3 fatty acids include alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), all of which are polyunsaturated. Salmon,

trout, and tuna are good sources of omega-3 fatty acids. Research indicates that omega-3 fatty acids reduce the risk of sudden death from heart attacks, reduce triglycerides in the blood, lower blood pressure, and prevent thrombosis by inhibiting blood clotting. They also reduce inflammation, and may help reduce the risk of some cancers in animals.

Like carbohydrates, fats have received a lot of bad publicity. It is true that eating an excess of fried foods and other “fatty” foods leads to weight gain. However, fats do have important functions. Many vitamins are fat soluble, and fats serve as a long-term storage form of fatty acids: a source of energy. They also provide insulation for the body. Therefore, “healthy” fats in moderate amounts should be consumed on a regular basis.

Waxes

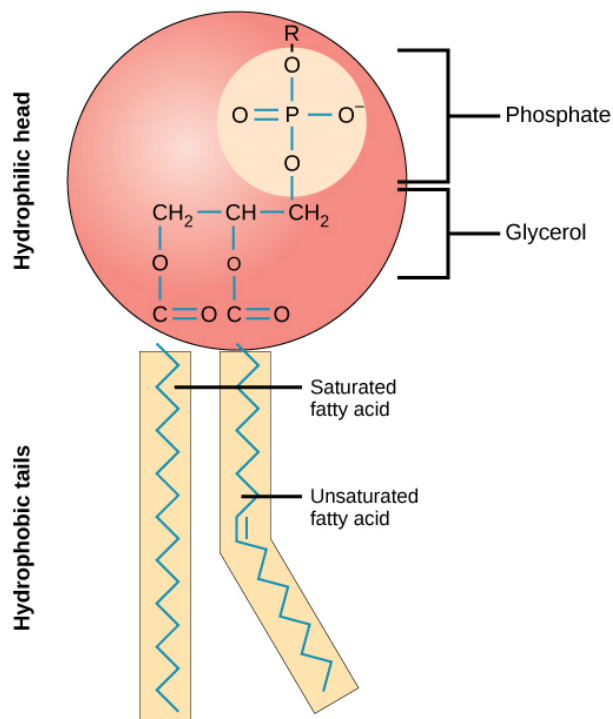
Wax covers the feathers of some aquatic birds and the leaf surfaces of some plants. Because of the hydrophobic nature of waxes, they prevent water from sticking on the surface ([link](#)). Waxes are made up of long fatty acid chains esterified to long-chain alcohols.



Waxy coverings on some leaves are made of lipids. (credit: Roger Griffith)

Phospholipids

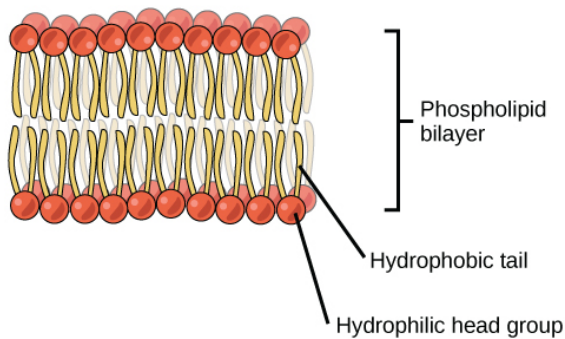
Phospholipids are major constituents of the plasma membrane, the outermost layer of animal cells. Like fats, they are composed of fatty acid chains attached to a glycerol or sphingosine backbone. Instead of three fatty acids attached as in triglycerides, however, there are two fatty acids forming diacylglycerol, and the third carbon of the glycerol backbone is occupied by a modified phosphate group ([\[link\]](#)). A phosphate group alone attached to a diacylglycerol does not qualify as a phospholipid; it is phosphatidate (diacylglycerol 3-phosphate), the precursor of phospholipids. The phosphate group is modified by an alcohol. Phosphatidylcholine and phosphatidylserine are two important phospholipids that are found in plasma membranes.



A phospholipid is a molecule with two fatty acids and a modified phosphate group attached to a

glycerol backbone. The phosphate may be modified by the addition of charged or polar chemical groups. Two chemical groups that may modify the phosphate, choline and serine, are shown here. Both choline and serine attach to the phosphate group at the position labeled R via the hydroxyl group indicated in green.

A phospholipid is an amphipathic molecule, meaning it has a hydrophobic and a hydrophilic part. The fatty acid chains are hydrophobic and cannot interact with water, whereas the phosphate-containing group is hydrophilic and interacts with water ([\[link\]](#)).



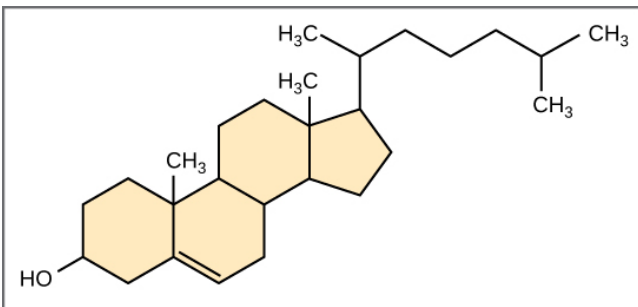
The phospholipid bilayer is the major component of all cellular membranes. The hydrophilic head groups of the phospholipids face the aqueous solution. The hydrophobic tails are sequestered in the middle of the bilayer.

The head is the hydrophilic part, and the tail contains the hydrophobic fatty acids. In a membrane, a bilayer of phospholipids forms the matrix of the structure, the fatty acid tails of phospholipids face inside, away from water, whereas the phosphate group faces the outside, aqueous side ([\[link\]](#)).

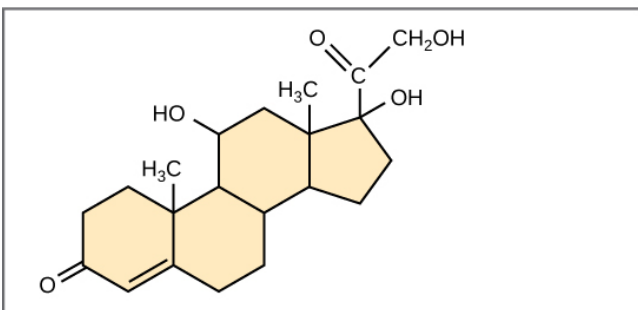
Phospholipids are responsible for the dynamic nature of the plasma membrane. If a drop of phospholipids is placed in water, it spontaneously forms a structure known as a micelle, where the hydrophilic phosphate heads face the outside and the fatty acids face the interior of this structure.

Steroids

Unlike the phospholipids and fats discussed earlier, **steroids** have a fused ring structure. Although they do not resemble the other lipids, they are grouped with them because they are also hydrophobic and insoluble in water. All steroids have four linked carbon rings and several of them, like cholesterol, have a short tail ([\[link\]](#)). Many steroids also have the -OH functional group, which puts them in the alcohol classification (sterols).



Cholesterol



Cortisol

Steroids such as cholesterol and cortisol are composed of four fused hydrocarbon rings.

Cholesterol is the most common steroid. Cholesterol is mainly synthesized in the liver and is the precursor to many steroid hormones such as testosterone and estradiol, which are secreted by the gonads and endocrine glands. It is also the precursor to Vitamin D. Cholesterol is also the precursor of bile salts, which help in the emulsification of fats and their subsequent absorption by cells. Although cholesterol is often spoken of in negative terms by lay people, it is necessary for proper functioning of the body. It is a component of the plasma membrane of animal cells and is found within the phospholipid bilayer. Being the outermost structure in animal cells, the plasma membrane is responsible for the transport of materials and cellular recognition and it is involved in cell-to-cell communication.

Note:

Link to Learning



For an additional perspective on lipids, explore the interactive animation [“Biomolecules: The Lipids”](#). For more information on lipids, please visit the UCD Chemwiki site at [Chemwiki lipids](#)

Another perspective on lipids, that contains a variety of animations to help you, is the following link from Carnegie Mellon University, Department of Biological Sciences flash tutorial on [lipids](#).

Exercise:

Problem: Which molecule makes up the bulk of a cell's membrane?

- a. polysachharides
- b. phospholipids
- c. monosaccharides
- d. proteins
- e. a and c
- f. b and d

Solution:

f

Exercise:

Problem: Which lipid is mainly used for energy storage?

- a. triglycerides
- b. steroids
- c. phospholipids
- d. waxes
- e. a and c
- f. b and d

Solution:

a

Section Summary

Lipids are a class of macromolecules that are nonpolar and hydrophobic in nature. Major types include fats and oils, waxes, phospholipids, and steroids. Fats are a stored form of energy and are also known as

triacylglycerols or triglycerides. Fats are made up of fatty acids and either glycerol or sphingosine. Fatty acids may be unsaturated or saturated, depending on the presence or absence of double bonds in the hydrocarbon chain. If only single bonds are present, they are known as saturated fatty acids. Unsaturated fatty acids may have one or more double bonds in the hydrocarbon chain. Phospholipids make up the matrix of membranes. They have a glycerol or sphingosine backbone to which two fatty acid chains and a phosphate-containing group are attached. Steroids are another class of lipids. Their basic structure has four fused carbon rings. Cholesterol is a type of steroid and is an important constituent of the plasma membrane, where it helps to maintain the fluid nature of the membrane. It is also the precursor of steroid hormones such as testosterone.

Review Questions

Exercise:

Problem:

Saturated fats have all of the following characteristics except:

- a. they are solid at room temperature
- b. they have single bonds within the carbon chain
- c. they are usually obtained from animal sources
- d. they tend to dissolve in water easily

Solution:

D

Exercise:

Problem: Phospholipids are important components of _____.

- a. the plasma membrane of animal cells
- b. the ring structure of steroids
- c. the waxy covering on leaves

d. the double bond in hydrocarbon chains

Solution:

A

Free Response

Exercise:

Problem:

Explain at least three functions that lipids serve in plants and/or animals.

Solution:

Fat serves as a valuable way for animals to store energy. It can also provide insulation. Waxes can protect plant leaves and mammalian fur from getting wet. Phospholipids and steroids are important components of animal cell membranes, as well as plant, fungal, and bacterial membranes.

Exercise:

Problem:

Why have trans fats been banned from some restaurants? How are they created?

Solution:

Trans fats are created artificially when hydrogen gas is bubbled through oils to solidify them. The double bonds of the *cis* conformation in the hydrocarbon chain may be converted to double bonds in the *trans* configuration. Some restaurants are banning trans fats because they cause higher levels of LDL, or “bad” cholesterol.

Glossary

lipid

macromolecule that is nonpolar and insoluble in water

omega fat

type of polyunsaturated fat that is required by the body; the numbering of the carbon omega starts from the methyl end or the end that is farthest from the carboxylic end

phospholipid

major constituent of the membranes; composed of two fatty acids and a phosphate-containing group attached to a glycerol backbone

saturated fatty acid

long-chain of hydrocarbon with single covalent bonds in the carbon chain; the number of hydrogen atoms attached to the carbon skeleton is maximized

steroid

type of lipid composed of four fused hydrocarbon rings forming a planar structure

trans fat

fat formed artificially by hydrogenating oils, leading to a different arrangement of double bond(s) than those found in naturally occurring lipids

triacylglycerol (also, triglyceride)

fat molecule; consists of three fatty acids linked to a glycerol molecule

unsaturated fatty acid

long-chain hydrocarbon that has one or more double bonds in the hydrocarbon chain

wax

lipid made of a long-chain fatty acid that is esterified to a long-chain alcohol; serves as a protective coating on some feathers, aquatic

mammal fur, and leaves

Bis2A 03.4 Nucleic Acids v1.2

By the end of this section, you will be able to:

- Describe the structure of nucleic acids and define the two types of nucleic acids
- Explain the structure and role of DNA
- Explain the structure and roles of RNA

NUCLEIC ACIDS

Nucleic acids carry the genetic blueprint of a cell and carry instructions for the functioning of the cell. In some instances, nucleic acids, primarily RNA, are also involved in catalysis and enzymatic activity. In such cases RNA-protein enzymes are often referred to as ribozymes and include such enzymes as RNaseP, the Ribosome, and the spliceosome.

DNA and RNA

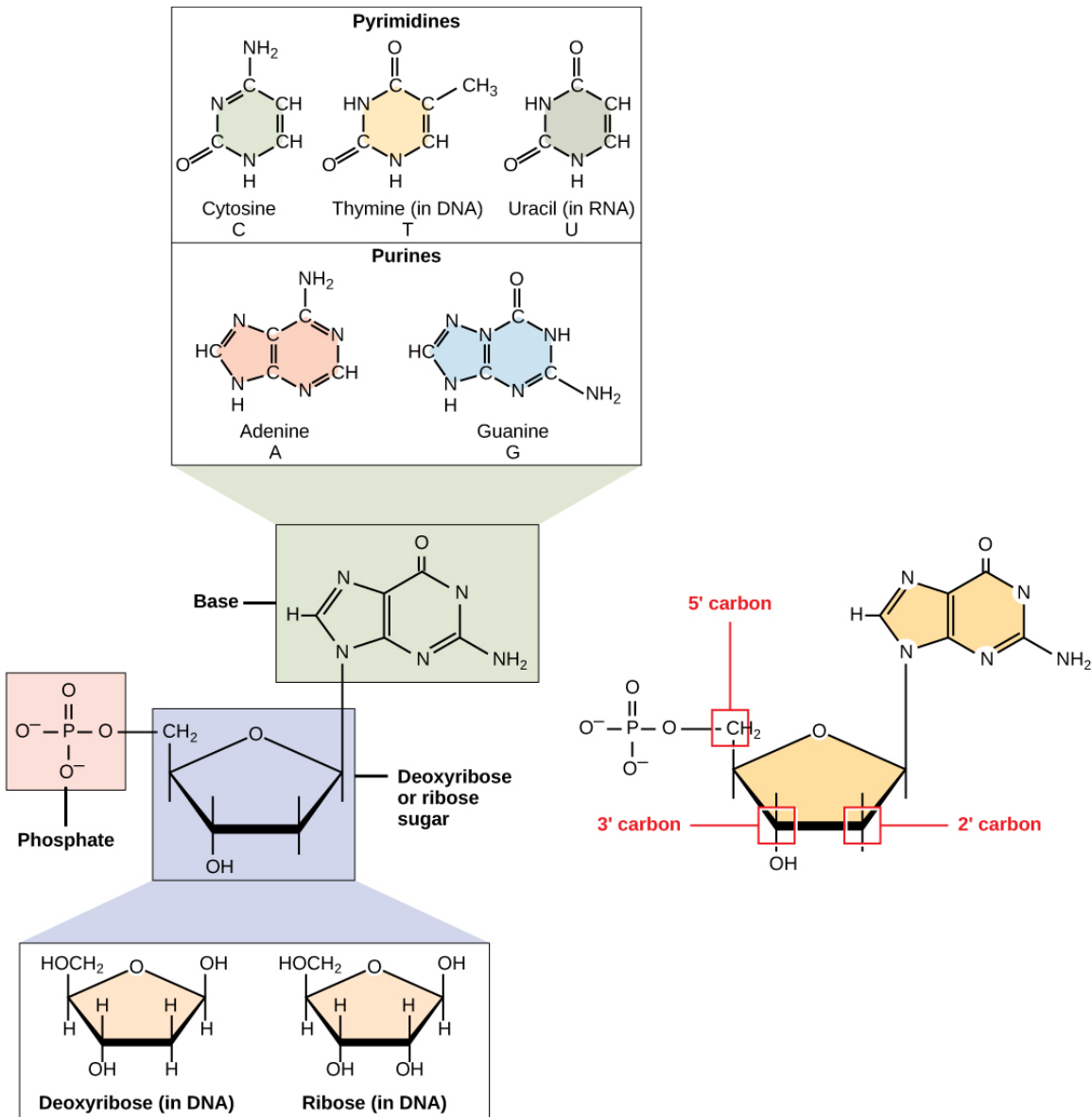
The two main types of nucleic acids are **deoxyribonucleic acid (DNA)** and **ribonucleic acid (RNA)**. DNA is the genetic material found in all living organisms, ranging from single-celled bacteria to multicellular mammals. It is found in the nucleus of eukaryotes and in the organelles, chloroplasts, and mitochondria and in the "nucleoid" in prokaryotes, that is bacteria and archaea, which is NOT enclosed in a membranous envelope. For a quick video (2 minutes) that goes over the differences of DNA and RNA click [here](#).

The entire genetic content of a cell is known as its genome, and the study of genomes is genomics. In eukaryotic cells but not in prokaryotes, DNA forms a complex with histone proteins to form chromatin, the substance of eukaryotic chromosomes. A chromosome may contain tens of thousands of genes. Many genes contain the information to make protein products; other genes code for RNA products. DNA controls all of the cellular activities by turning the genes "on" or "off."

The other type of nucleic acid, RNA, is mostly involved in protein synthesis. The DNA molecules never leave the nucleus but instead use an

intermediary to communicate with the rest of the cell. This intermediary is the **messenger RNA (mRNA)**. Other types of RNA—like rRNA, tRNA, and microRNA—are involved in protein synthesis and its regulation.

DNA and RNA are made up of monomers known as **nucleotides**. The nucleotides combine with each other to form a **polynucleotide**, DNA or RNA. Each nucleotide is made up of three components: a nitrogenous base, a pentose (five-carbon) sugar, and a phosphate group ([\[link\]](#)). Each nitrogenous base in a nucleotide is attached to a sugar molecule, which is attached to one or more phosphate groups.



A nucleotide is made up of three components: a nitrogenous base, a pentose sugar, and one or more phosphate groups. Carbon residues in the pentose are numbered 1' through 5' (the prime distinguishes these residues from those in the base, which are numbered without using a prime notation). The base is attached to the 1' position of the ribose, and the phosphate is attached to the 5' position. When a polynucleotide is formed, the 5' phosphate of the incoming nucleotide attaches to the 3' hydroxyl group at the end of the growing chain. Two types of pentose are found in nucleotides, deoxyribose (found in DNA) and ribose (found in RNA). Deoxyribose is similar in structure

to ribose, but it has an H instead of an OH at the 2' position. Bases can be divided into two categories: purines and pyrimidines. Purines have a double ring structure, and pyrimidines have a single ring.

The nitrogenous bases, important components of nucleotides, are organic molecules and are so named because they contain carbon and nitrogen. They are bases because they contain an amino group that has the potential of binding an extra hydrogen, and thus, decreases the hydrogen ion concentration in its environment, making it more basic. Each nucleotide in DNA contains one of four possible nitrogenous bases: adenine (A), guanine (G) cytosine (C), and thymine (T).

Adenine and guanine are classified as **purines**. The primary structure of a purine is two carbon-nitrogen rings. Cytosine, thymine, and uracil are classified as **pyrimidines** which have a single carbon-nitrogen ring as their primary structure ([\[link\]](#)). Each of these basic carbon-nitrogen rings has different functional groups attached to it. In molecular biology shorthand, the nitrogenous bases are simply known by their symbols A, T, G, C, and U. DNA contains A, T, G, and C whereas RNA contains A, U, G, and C.

The pentose sugar in DNA is deoxyribose, and in RNA, the sugar is ribose ([\[link\]](#)). The difference between the sugars is the presence of the hydroxyl group on the second carbon of the ribose and hydrogen on the second carbon of the deoxyribose. The carbon atoms of the sugar molecule are numbered as 1', 2', 3', 4', and 5' (1' is read as "one prime"). The phosphate residue is attached to the hydroxyl group of the 5' carbon of one sugar and the hydroxyl group of the 3' carbon of the sugar of the next nucleotide, which forms a 5'–3' **phosphodiester** linkage. The phosphodiester linkage is not formed by simple dehydration reaction like the other linkages connecting monomers in macromolecules: its formation involves the removal of two phosphate groups. A polynucleotide may have thousands of such phosphodiester linkages.

Exercise:

Problem:

Which of these is NOT a difference between DNA and RNA?

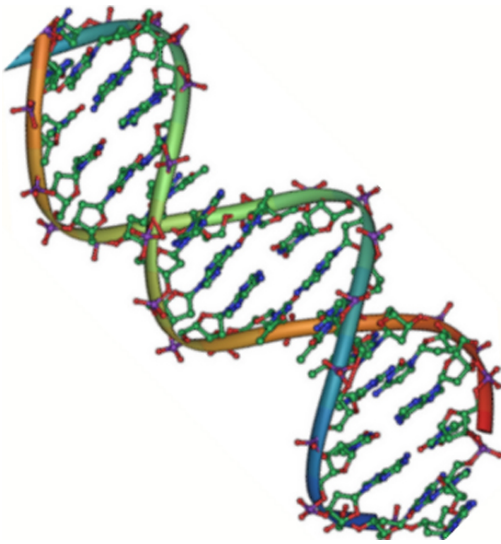
- a. DNA tends to be double stranded, while RNA tends to be single stranded
- b. RNA uses the base thymine while DNA uses the base uracil.
- c. phospholipids
- d. DNA uses the sugar deoxyribose while RNA uses the sugar ribose.
- e. All of these are differences between DNA and RNA.

Solution:

B

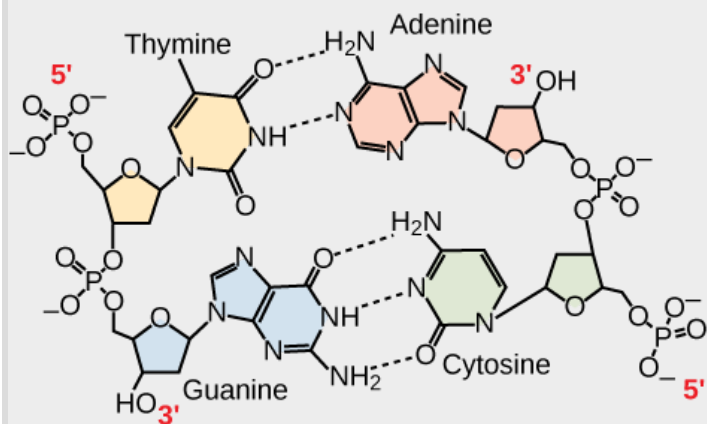
DNA Double-Helix Structure

DNA has a double-helix structure ([\[link\]](#)). The sugar and phosphate lie on the outside of the helix, forming the backbone of the DNA. The nitrogenous bases are stacked in the interior, like the steps of a staircase, in pairs; the pairs are bound to each other by hydrogen bonds. Every base pair in the double helix is separated from the next base pair by 0.34 nm. The two strands of the helix run in opposite directions, meaning that the 5' carbon end of one strand will face the 3' carbon end of its matching strand. This is referred to as antiparallel orientation. It is important to DNA replication and in many nucleic acid interactions.



Native DNA is an antiparallel double helix. The phosphate backbone (indicated by the curvy lines) is on the outside, and the bases are on the inside. Each base from one strand interacts via hydrogen bonding with a base from the opposing strand. (credit: Jerome Walker/Dennis Myts)

Only certain types of base pairing are allowed. For example, a certain purine can only pair with a certain pyrimidine. This means A can pair with T, and G can pair with C, as shown in [\[link\]](#). This is known as the base complementary rule. In other words, the DNA strands are complementary to each other. If the sequence of one strand is AATTGGCC, the complementary strand would have the sequence TTAACCGG. During DNA replication, each strand is copied, resulting in a daughter DNA double helix containing one parental DNA strand and a newly synthesized strand.

Note:**Art Connection**

In a double stranded DNA molecule, the two strands run antiparallel to one another so that one strand runs 5' to 3' and the other 3' to 5'. The phosphate backbone is located on the outside, and the bases are in the middle.

Adenine forms hydrogen bonds (or base pairs) with thymine, and guanine base pairs with cytosine.

A mutation occurs, and cytosine is replaced with adenine. What impact do you think this will have on the DNA structure?

Exercise:**Problem:**

Using figure 5.3 above. What functional group is the 3' end of the nucleic acid referring to?

- a. Phosphate group
- b. the nitrogenous base
- c. the ribose sugar
- d. the hydroxyl (OH group)

Solution:

D

Exercise:**Problem:**

Using the figure 3 above, which functional group is the 5' referring to?

- a. Phosphate group
- b. the nitrogenous base
- c. the ribose sugar
- d. the hydroxyl (OH group)

Solution:

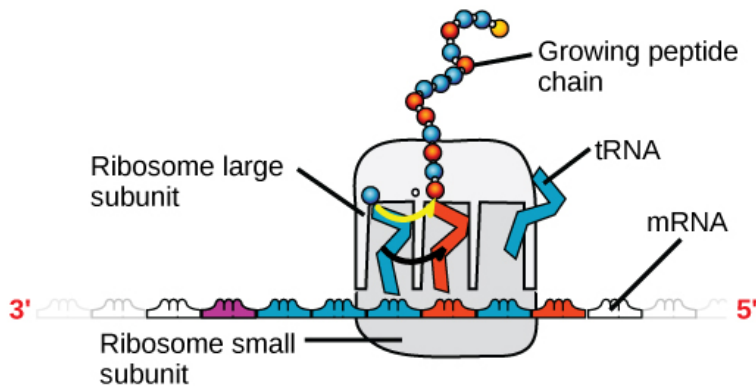
a

RNA

Ribonucleic acid, or RNA, is mainly involved in the process of protein synthesis under the direction of DNA. RNA is usually single-stranded and is made of ribonucleotides that are linked by phosphodiester bonds. A ribonucleotide in the RNA chain contains ribose (the pentose sugar), one of the four nitrogenous bases (A, U, G, and C), and the phosphate group.

There are four major types of RNA: messenger RNA (mRNA), ribosomal RNA (rRNA), transfer RNA (tRNA), and microRNA (miRNA). The first, mRNA, carries the message from DNA, which controls all of the cellular activities in a cell. If a cell requires a certain protein to be synthesized, the gene for this product is turned “on” and the messenger RNA is synthesized in the nucleus. The RNA base sequence is complementary to the coding sequence of the DNA from which it has been copied. However, in RNA, the base T is absent and U is present instead. If the DNA strand has a sequence

AATTGCGC, the sequence of the complementary RNA is UUAACGCG. In the cytoplasm, the mRNA interacts with ribosomes and other cellular machinery ([link](#)).



A ribosome has two parts: a large subunit and a small subunit. The mRNA sits in between the two subunits. A tRNA molecule recognizes a codon on the mRNA, binds to it by complementary base pairing, and adds the correct amino acid to the growing peptide chain.

The mRNA is read in sets of three bases known as codons. Each codon codes for a single amino acid. In this way, the mRNA is read and the protein product is made. **Ribosomal RNA (rRNA)** is a major constituent of ribosomes on which the mRNA binds. The rRNA ensures the proper alignment of the mRNA and the ribosomes; the rRNA of the ribosome also has an enzymatic activity (peptidyl transferase) and catalyzes the formation of the peptide bonds between two aligned amino acids. **Transfer RNA (tRNA)** is one of the smallest of the four types of RNA, usually 70–90 nucleotides long. It carries the correct amino acid to the site of protein synthesis. It is the base pairing between the tRNA and mRNA that allows for the correct amino acid to be inserted in the polypeptide chain. microRNAs are the smallest RNA molecules and their role involves the

regulation of gene expression by interfering with the expression of certain mRNA messages. [\[link\]](#) summarizes features of DNA and RNA.

Features of DNA and RNA		
	DNA	RNA
Function	Carries genetic information	Involved in protein synthesis
Location	Remains in the nucleus	Leaves the nucleus
Structure	Double helix	Usually single-stranded
Sugar	Deoxyribose	Ribose
Pyrimidines	Cytosine, thymine	Cytosine, uracil
Purines	Adenine, guanine	Adenine, guanine

Even though the RNA is single stranded, most RNA types show extensive intramolecular base pairing between complementary sequences, creating a predictable three-dimensional structure essential for their function.

As you have learned, information flow in an organism takes place from DNA to RNA to protein. DNA dictates the structure of mRNA in a process known as **transcription**, and RNA dictates the structure of protein in a process known as **translation**. This is known as the Central Dogma of Life, which holds true for all organisms; however, exceptions to the rule occur in connection with viral infections.

Note:

Link to Learning



To learn more about DNA, explore the [Howard Hughes Medical Institute BioInteractive animations](#) on the topic of DNA.

Section Summary

Nucleic acids are molecules made up of nucleotides that direct cellular activities such as cell division and protein synthesis. Each nucleotide is made up of a pentose sugar, a nitrogenous base, and a phosphate group. There are two types of nucleic acids: DNA and RNA. DNA carries the genetic blueprint of the cell and is passed on from parents to offspring (in the form of chromosomes). It has a double-helical structure with the two strands running in opposite directions, connected by hydrogen bonds, and complementary to each other. RNA is single-stranded and is made of a pentose sugar (ribose), a nitrogenous base, and a phosphate group. RNA is involved in protein synthesis and its regulation. Messenger RNA (mRNA) is copied from the DNA, is exported from the nucleus to the cytoplasm, and contains information for the construction of proteins. Ribosomal RNA (rRNA) is a part of the ribosomes at the site of protein synthesis, whereas transfer RNA (tRNA) carries the amino acid to the site of protein synthesis. microRNA regulates the use of mRNA for protein synthesis.

Art Connections

Exercise:

Problem:

[\[link\]](#) A mutation occurs, and cytosine is replaced with adenine. What impact do you think this will have on the DNA structure?

Solution:

[\[link\]](#) Adenine is larger than cytosine and will not be able to base pair properly with the guanine on the opposing strand. This will cause the DNA to bulge. DNA repair enzymes may recognize the bulge and replace the incorrect nucleotide.

Review Questions

Exercise:

Problem: A nucleotide of DNA may contain _____.

- a. ribose, uracil, and a phosphate group
- b. deoxyribose, uracil, and a phosphate group
- c. deoxyribose, thymine, and a phosphate group
- d. ribose, thymine, and a phosphate group

Solution:

C

Exercise:

Problem: The building blocks of nucleic acids are _____.

- a. sugars
- b. nitrogenous bases
- c. peptides
- d. nucleotides

Solution:

D

Free Response**Exercise:**

Problem:What are the structural differences between RNA and DNA?

Solution:

DNA has a double-helix structure. The sugar and the phosphate are on the outside of the helix and the nitrogenous bases are in the interior. The monomers of DNA are nucleotides containing deoxyribose, one of the four nitrogenous bases (A, T, G and C), and a phosphate group. RNA is usually single-stranded and is made of ribonucleotides that are linked by phosphodiester linkages. A ribonucleotide contains ribose (the pentose sugar), one of the four nitrogenous bases (A,U, G, and C), and the phosphate group.

Exercise:

Problem:What are the four types of RNA and how do they function?

Solution:

The four types of RNA are messenger RNA, ribosomal RNA, transfer RNA, and microRNA. Messenger RNA carries the information from the DNA that controls all cellular activities. The mRNA binds to the ribosomes that are constructed of proteins and rRNA, and tRNA transfers the correct amino acid to the site of protein synthesis. microRNA regulates the availability of mRNA for translation.

Glossary

deoxyribonucleic acid (DNA)

double-helical molecule that carries the hereditary information of the cell

messenger RNA (mRNA)

RNA that carries information from DNA to ribosomes during protein synthesis

nucleic acid

biological macromolecule that carries the genetic blueprint of a cell and carries instructions for the functioning of the cell

nucleotide

monomer of nucleic acids; contains a pentose sugar, one or more phosphate groups, and a nitrogenous base

phosphodiester

linkage covalent chemical bond that holds together the polynucleotide chains with a phosphate group linking two pentose sugars of neighboring nucleotides

polynucleotide

long chain of nucleotides

purine

type of nitrogenous base in DNA and RNA; adenine and guanine are purines

pyrimidine

type of nitrogenous base in DNA and RNA; cytosine, thymine, and uracil are pyrimidines

ribonucleic acid (RNA)

single-stranded, often internally base paired, molecule that is involved in protein synthesis

ribosomal RNA (rRNA)

RNA that ensures the proper alignment of the mRNA and the ribosomes during protein synthesis and catalyzes the formation of the peptide linkage

transcription

process through which messenger RNA forms on a template of DNA

transfer RNA (tRNA)

RNA that carries activated amino acids to the site of protein synthesis on the ribosome

translation

process through which RNA directs the formation of protein

Bis2A 03.5 Synthesis of Biological Macromolecules

By the end of this section, you will be able to:

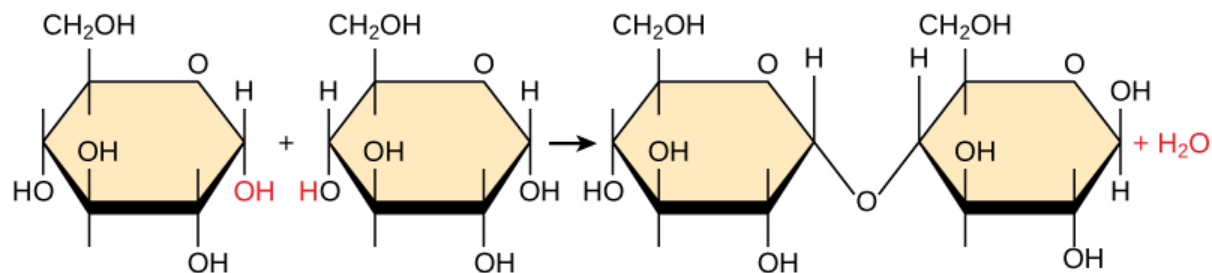
- Understand the synthesis of macromolecules
- Explain dehydration (or condensation) and hydrolysis reactions

BIO SYNTHESIS AND DEGRADATION

As you've learned, **biological macromolecules** are large molecules, necessary for life, that are built from smaller organic molecules. There are four major classes of biological macromolecules (carbohydrates, lipids, proteins, and nucleic acids); each is an important cell component and performs a wide array of functions. Combined, these molecules make up the majority of a cell's dry mass (recall that water makes up the majority of its complete mass). Biological macromolecules are organic, meaning they contain carbon. In addition, they may contain hydrogen, oxygen, nitrogen, and additional minor elements.

Dehydration Synthesis

Most macromolecules are made from single subunits, or building blocks, called **monomers**. The monomers combine with each other using covalent bonds to form larger molecules known as **polymers**. In doing so, monomers release water molecules as byproducts. This type of reaction is known as **dehydration synthesis**, which means “to put together while losing water.”



In the dehydration synthesis reaction depicted above, two molecules of glucose are linked together to form the disaccharide maltose. In the

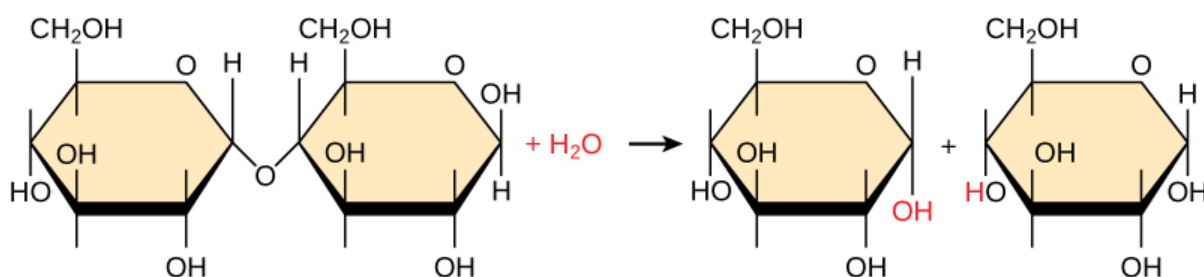
process, a water molecule is formed.

In a dehydration synthesis reaction ([\[link\]](#)), the hydrogen of one monomer combines with the hydroxyl group of another monomer, releasing a molecule of water. At the same time, the monomers share electrons and form covalent bonds. As additional monomers join, this chain of repeating monomers forms a polymer. Different types of monomers can combine in many configurations, giving rise to a diverse group of macromolecules. Even one kind of monomer can combine in a variety of ways to form several different polymers: for example, glucose monomers are the constituents of starch, glycogen, and cellulose.

While we just saw how carbohydrate monomers are added to a polymer by dehydration reaction, this type of reaction is used to add amino acids to growing peptide chains, fatty acids to the glycerol backbone and nucleotides to the growing DNA or RNA polymer. Go back to the modules on Proteins, Lipids, and Nucleic Acids and see if you can identify the water molecules that are removed when a monomer is added to the growing polymer

Hydrolysis

Polymers are broken down into monomers in a process known as hydrolysis, which means “to split water,” a reaction in which a water molecule is used during the breakdown ([\[link\]](#)). During these reactions, the polymer is broken into two components: one part gains a hydrogen atom (H^+) and the other gains a hydroxyl molecule (OH^-) from a split water molecule.



In the hydrolysis reaction shown here, the disaccharide maltose is broken down to form two glucose monomers with the addition of a water molecule. Note that this reaction is the reverse of the synthesis reaction shown in [\[link\]](#).

Dehydration and **hydrolysis reactions** are catalyzed, or “sped up,” by specific enzymes; dehydration reactions involve the formation of new bonds, requiring energy, while hydrolysis reactions break bonds and release energy. These reactions are similar for most macromolecules, but each monomer and polymer reaction is specific for its class. For example, in our bodies, food is hydrolyzed, or broken down, into smaller molecules by catalytic enzymes in the digestive system. This allows for easy absorption of nutrients by cells in the intestine. Each macromolecule is broken down by a specific enzyme. For instance, carbohydrates are broken down by amylase, sucrase, lactase, or maltase. Proteins are broken down by the enzymes pepsin and peptidase, and by hydrochloric acid. Lipids are broken down by lipases. Breakdown of these macromolecules provides energy for cellular activities.

Note:

Link to Learning



Visit [this site](#) to see visual representations of dehydration synthesis and hydrolysis.

Example of Hydrolysis with Enzyme Action is shown in this 3 minute video entitled: [hydrolysis of sucrose by sucrase](#).

Section Summary

Proteins, carbohydrates, nucleic acids, and lipids are the four major classes of biological macromolecules—large molecules necessary for life that are built from smaller organic molecules. Macromolecules are made up of single units known as monomers that are joined by covalent bonds to form larger polymers. The polymer is more than the sum of its parts: it acquires new characteristics, and leads to an osmotic pressure that is much lower than that formed by its ingredients; this is an important advantage in the maintenance of cellular osmotic conditions. A monomer joins with another monomer with the release of a water molecule, leading to the formation of a covalent bond. These types of reactions are known as dehydration or condensation reactions. When polymers are broken down into smaller units (monomers), a molecule of water is used for each bond broken by these reactions; such reactions are known as hydrolysis reactions. Dehydration and hydrolysis reactions are similar for all macromolecules, but each monomer and polymer reaction is specific to its class. Dehydration reactions typically require an investment of energy for new bond formation, while hydrolysis reactions typically release energy by breaking bonds.

Review Questions

Exercise:

Problem: Dehydration synthesis leads to formation of

- a. monomers
- b. polymers
- c. water and polymers
- d. none of the above

Solution:

C

Exercise:

Problem:

During the breakdown of polymers, which of the following reactions takes place?

- a. hydrolysis
- b. dehydration
- c. condensation
- d. covalent bond

Solution:

A

Free Response

Exercise:

Problem: Why are biological macromolecules considered organic?

Solution:

Biological macromolecules are organic because they contain carbon.

Exercise:

Problem:

What role do electrons play in dehydration synthesis and hydrolysis?

Solution:

In a dehydration synthesis reaction, the hydrogen of one monomer combines with the hydroxyl group of another monomer, releasing a molecule of water. This creates an opening in the outer shells of atoms in the monomers, which can share electrons and form covalent bonds.

Glossary

biological macromolecule

large molecule necessary for life that is built from smaller organic molecules

dehydration synthesis

(also, condensation) reaction that links monomer molecules together, releasing a molecule of water for each bond formed

hydrolysis

reaction causes breakdown of larger molecules into smaller molecules with the utilization of water

monomer

smallest unit of larger molecules called polymers

polymer

chain of monomer residues that is linked by covalent bonds;
polymerization is the process of polymer formation from monomers by condensation

Bis2A 04.0 Energy and Thermodynamics v1.2

By the end of this section, you will be able to:

- Define “energy”
- Explain the difference between kinetic and potential energy
- Discuss the concepts of free energy and activation energy
- Describe endergonic and exergonic reactions

INTRODUCTION TO ENERGY

Energy is the ability to do **work**. Work is done when a force is applied to an object over a distance. When an object is in motion, there is energy associated with that object. In the example of an airplane in flight, there is a great deal of energy associated with the motion of the airplane. This is because moving objects are capable of enacting a change, or doing work. Think of a wrecking ball. Even a slow-moving wrecking ball can do a great deal of damage to other objects. However, a wrecking ball that is not in motion is incapable of performing work. Energy associated with objects in motion is called **kinetic energy**. A speeding bullet, a walking person, the rapid movement of molecules in the air (which produces heat), and electromagnetic radiation like light all have kinetic energy. Any moving object has kinetic energy and thus can do work. Similarly, work has to be done on an object to change its kinetic energy. The kinetic energy of an object of mass m and speed v is given by the relation $E = 1/2mv^2$.

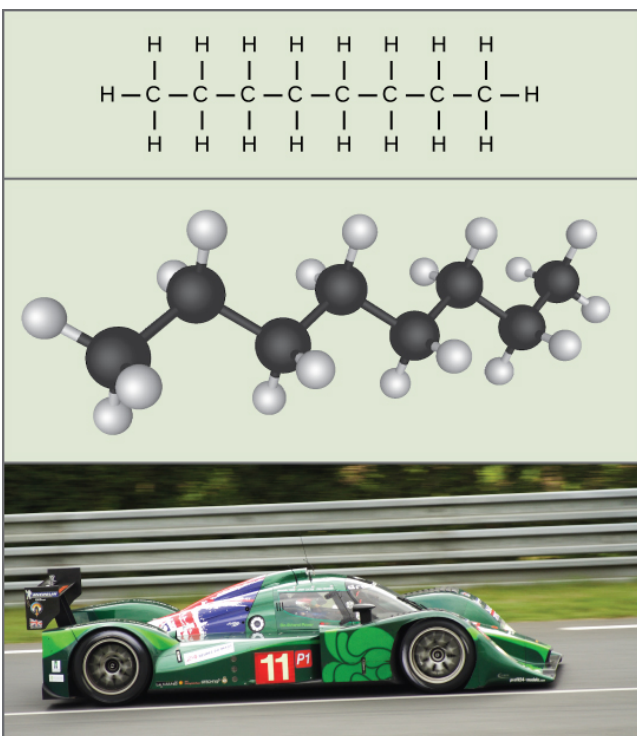
Sometimes energy can be stored and used at a later time. For example, a compressed spring and water held back by a dam both have the potential to do work ([\[link\]](#)). They are said to possess **potential energy**. When the spring or water is released its potential energy is transformed into kinetic energy and other forms of energy such as heat. Remember that wrecking ball described above moving, even slowly has kinetic energy. What if it is motionless, lying on the ground; does it possess any form of energy? Now what if that same motionless wrecking ball is lifted two stories above a car with a crane? If the suspended wrecking ball is unmoving, is there energy associated with it? The answer is yes. The suspended wrecking ball has energy associated with it that is fundamentally different from the kinetic energy of objects in motion. This form of energy results from the fact that

there is the *potential* for the wrecking ball to do work. If it is released, indeed it would do work. Because this type of energy refers to the potential to do work, it is called **potential energy**. Objects transfer their energy between kinetic and potential in the following way: As the wrecking ball hangs motionless, it has 0 kinetic and 100 percent potential energy. Once it is released, its kinetic energy begins to increase because it builds speed due to gravity. At the same time, as it nears the ground, it loses potential energy. Somewhere mid-fall it has 50 percent kinetic and 50 percent potential energy. Just before it hits the ground, the ball has nearly lost its potential energy and has near-maximal kinetic energy. The energy associated to the gravitational force near the surface of the earth is potential energy. Other forms of energy are really combinations of kinetic and potential energy. For example, chemical energy, is the electrical potential energy stored in atoms. Heat energy is a combination of the potential and kinetic energy of the particles in a substance.



Water behind a dam has potential energy. Moving water, such as in a waterfall or a rapidly flowing river, has kinetic energy. (credit “dam”: modification of work by "Pascal"/Flickr; credit “waterfall”: modification of work by Frank Gualtieri)

Potential energy is not only associated with the location of matter (such as a child sitting on a tree branch), but also with the structure of matter. A spring on the ground has potential energy if it is compressed; so does a rubber band that is pulled taut. The very existence of living cells relies heavily on structural potential energy. On a chemical level, the bonds that hold the atoms of molecules together have potential energy. Remember that anabolic cellular pathways require energy to synthesize complex molecules from simpler ones, and catabolic pathways release energy when complex molecules are broken down. The fact that energy can be released by the breakdown of certain chemical bonds implies that those bonds have potential energy. In fact, there is potential energy stored within the bonds of all the food molecules we eat, which is eventually harnessed for use. This is because these bonds can release energy when broken. The type of potential energy that exists within chemical bonds, and is released when those bonds are broken, is called **chemical energy** ([link](#)). Chemical energy is responsible for providing living cells with energy from food. The release of energy is brought about by breaking the molecular bonds within fuel molecules.



The molecules in gasoline (octane, the chemical formula shown) contain chemical energy within the chemical bonds. This energy is transformed into kinetic energy that allows a car to race on a racetrack. (credit “car”: modification of work by Russell Trow)

Note:

Link to Learning



Visit this [site](#) and select “A simple pendulum” on the menu (under “Harmonic Motion”) to see the shifting kinetic (K) and potential energy (U) of a pendulum in motion.

Forms of Energy

Mechanical energy puts something in motion. It moves cars and lifts elevators. A machine uses mechanical energy to do work. The mechanical energy of a system is the sum of its kinetic and potential energy. Levers, which need a fulcrum to operate, are the simplest type of machine. Wheels, pulleys and inclined planes are the basic elements of most machines.

Chemical energy is the energy stored in molecules and chemical compounds, and is found in food, wood, coal, petroleum and other fuels. When the chemical bonds are broken, either by combustion or other chemical reactions, the stored chemical energy is released in the form of heat or light. For example, muscle cells contain glycogen. When the muscle does work the glycogen is broken down into glucose. When the chemical energy in the glucose is transferred to the muscle fibers some of the energy goes into the surroundings as heat.

Electrical energy is produced when unbalanced forces between electrons and protons in atoms create moving electrons called electric currents. For example, when we spin a copper wire through the poles of a magnet we induce the motion of electrons in the wire and produce electricity. Electricity can be used to perform work such as lighting a bulb, heating a cooking element on a stove or powering a motor. Note that electricity is a "secondary" source of energy. That means other sources of energy are needed to produce electricity.

Radiant energy is carried by waves. Changes in the internal energy of particles cause the atoms to emit energy in the form of electromagnetic radiation which includes visible light, ultraviolet (UV) radiation, infrared (IR) radiation, microwaves, radio waves, gamma rays, and X-rays. Electromagnetic radiation from the sun, particularly light, is of utmost importance in environmental systems because biogeochemical cycles and virtually all other processes on earth are driven by them.

Thermal energy or **Heat energy** is related to the motion or vibration of molecules in a substance. When a thermal system changes, heat flows in or out of the system. Heat energy flows from hot bodies to cold ones. Heat flow, like work, is an energy transfer. When heat flows into a substance it may increase the kinetic energy of the particles and thus elevate its temperature. Heat flow may also change the arrangement of the particles making up a substance by increasing their potential energy. This is what happens to water when it reaches a temperature of 100°C. The molecules of water move further away from each other, thereby changing the state of the water from a liquid to a gas. During the phase transition the temperature of the water does not change.

Nuclear Energy is energy that comes from the binding of the protons and neutrons that make up the nucleus of the atoms. It can be released from atoms in two different ways: nuclear fusion or nuclear fission. In **nuclear fusion**, energy is released when atoms are combined or fused together. This is how the sun produces energy. In **nuclear fission**, energy is released when atoms are split apart. Nuclear fission is used in nuclear power plants to produce electricity. Uranium 235 is the fuel used in most nuclear power plants because it undergoes a chain reaction extremely rapidly, resulting in the fission of trillions of atoms within a fraction of a second.

Free Energy

After learning that chemical reactions release energy when energy-storing bonds are broken, an important next question is how is the energy associated with chemical reactions quantified and expressed? How can the energy released from one reaction be compared to that of another reaction? A measurement of **free energy** is used to quantitate these energy transfers. Free energy is called Gibbs free energy (abbreviated with the letter G) after Josiah Willard Gibbs, the scientist who developed the measurement. Recall that according to the second law of thermodynamics, all energy transfers involve the loss of some amount of energy in an unusable form such as heat, resulting in entropy. Gibbs free energy specifically refers to the energy associated with a chemical reaction that is available after entropy is accounted for. In other words, Gibbs free energy is usable energy, or energy that is available to do work.

Every chemical reaction involves a change in free energy, called delta G (ΔG). The change in free energy can be calculated for any system that undergoes such a change, such as a chemical reaction. To calculate ΔG , subtract the amount of energy lost to entropy (denoted as ΔS) from the total energy change of the system. This total energy change in the system is called **enthalpy** and is denoted as ΔH . The formula for calculating ΔG is as follows, where the symbol T refers to absolute temperature in Kelvin (degrees Celsius + 273):

Equation:

$$\Delta G = \Delta H - T\Delta S$$

The standard free energy change of a chemical reaction is expressed as an amount of energy per mole of the reaction product (either in kilojoules or kilocalories, kJ/mol or kcal/mol; 1 kJ = 0.239 kcal) under standard pH, temperature, and pressure conditions. Standard pH, temperature, and pressure conditions are generally calculated at pH 7.0 in biological systems, 25 degrees Celsius, and 100 kilopascals (1 atm pressure), respectively. It is important to note that cellular conditions vary considerably from these standard conditions, and so standard calculated ΔG values for biological reactions will be different inside the cell.

Endergonic Reactions and Exergonic Reactions

If energy is released during a chemical reaction, then the resulting value from the above equation will be a negative number. In other words, reactions that release energy have a $\Delta G < 0$. A negative ΔG also means that the products of the reaction have less free energy than the reactants, because they gave off some free energy during the reaction. Reactions that have a negative ΔG and consequently release free energy are called **exergonic reactions**. Think: *exergonic* means energy is *exiting* the system. These reactions are also referred to as spontaneous reactions, because they can occur without the addition of energy into the system. Understanding which chemical reactions are spontaneous and release free energy is extremely useful for biologists, because these reactions can be harnessed to perform work inside the cell. An important distinction must be drawn between the term spontaneous and the idea of a chemical reaction that occurs immediately. Contrary to the everyday use of the term, a spontaneous reaction is not one that suddenly or quickly occurs. The rusting of iron is an example of a spontaneous reaction that occurs slowly, little by little, over time.

If a chemical reaction requires an input of energy rather than releasing energy, then the ΔG for that reaction will be a positive value. In this case, the products have more free energy than the reactants. Thus, the products of these reactions can be thought of as energy-storing molecules. These

chemical reactions are called **endergonic reactions**, and they are non-spontaneous. An endergonic reaction will not take place on its own without the addition of free energy.

Let's revisit the example of the synthesis and breakdown of the food molecule, glucose. Remember that the building of complex molecules, such as sugars, from simpler ones is an anabolic process and requires energy. Therefore, the chemical reactions involved in anabolic processes are endergonic reactions. On the other hand, the catabolic process of breaking sugar down into simpler molecules releases energy in a series of exergonic reactions. Like the example of rust above, the breakdown of sugar involves spontaneous reactions, but these reactions don't occur instantaneously. [\[link\]](#) shows some other examples of endergonic and exergonic reactions. Later sections will provide more information about what else is required to make even spontaneous reactions happen more efficiently.

Note:

Art Connection



(a)



(b)



(c)



(d)

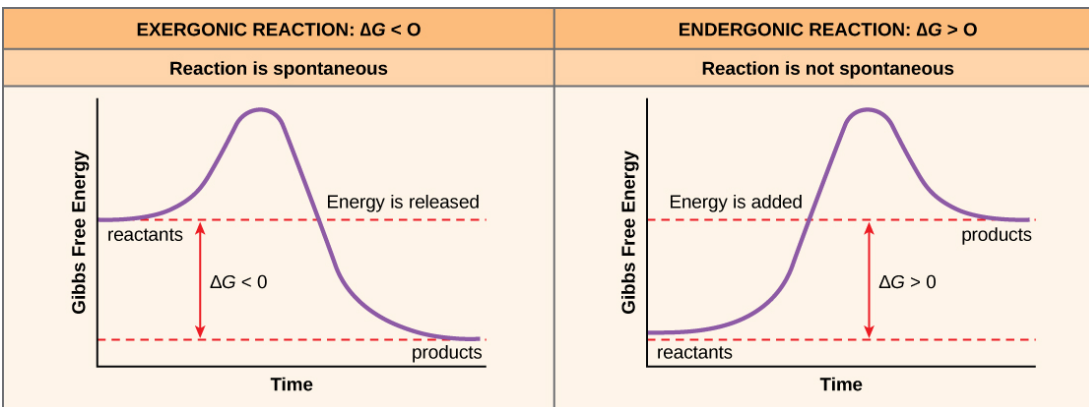
Shown are some examples of endergonic processes (ones that require energy) and

exergonic processes (ones that release energy). These include (a) a compost pile decomposing, (b) a chick hatching from a fertilized egg, (c) sand art being destroyed, and (d) a ball rolling down a hill. (credit a: modification of work by Natalie Maynor; credit b: modification of work by USDA; credit c: modification of work by “Athlex”/Flickr; credit d: modification of work by Harry Malsch)

Look at each of the processes shown, and decide if it is endergonic or exergonic. In each case, does enthalpy increase or decrease, and does entropy increase or decrease?

An important concept in the study of metabolism and energy is that of chemical equilibrium. Most chemical reactions are reversible. They can proceed in both directions, releasing energy into their environment in one direction, and absorbing it from the environment in the other direction ([link](#)). The same is true for the chemical reactions involved in cell metabolism, such as the breaking down and building up of proteins into and from individual amino acids, respectively. Reactants within a closed system will undergo chemical reactions in both directions until a state of equilibrium is reached. This state of equilibrium is one of the lowest possible free energy and a state of maximal entropy. Energy must be put into the system to push the reactants and products away from a state of equilibrium. Either reactants or products must be added, removed, or changed. If a cell were a closed system, its chemical reactions would reach equilibrium, and it would die because there would be insufficient free energy left to perform the work needed to maintain life. In a living cell, chemical reactions are constantly moving towards equilibrium, but never reach it. This is because a living cell is an open system. Materials pass in and out, the cell recycles the products of certain chemical reactions into other reactions, and chemical equilibrium is never reached. In this way,

living organisms are in a constant energy-requiring, uphill battle against equilibrium and entropy. This constant supply of energy ultimately comes from sunlight, which is used to produce nutrients in the process of photosynthesis.



Exergonic and endergonic reactions result in changes in Gibbs free energy. Exergonic reactions release energy; endergonic reactions require energy to proceed.

Exercise:
Reading Energy Diagrams

Problem:

Use figure 4 above. In exergonic reactions, the products have:

- a. more energy than the reactants
- b. less energy than the reactants
- c. are always the higher energy compounds
- d. are always the lower energy compounds
- e. a and c
- f. b and d

Solution:

b

Exercise:

Problem:

Use figure 4 above. The information in the ΔG of a reaction:

- a. tells you the rate of the reaction
- b. tells you if it is exergonic or endergonic
- c. tells if the reaction has reached equilibrium
- d. tells the the amount of energy difference between the reactants and products
- e. a and b
- f. a and c
- g. a and d
- h. b and c
- i. b and d

Solution:

i

Activation Energy

There is another important concept that must be considered regarding endergonic and exergonic reactions. Even exergonic reactions require a small amount of energy input to get going before they can proceed with their energy-releasing steps. These reactions have a net release of energy, but still require some energy in the beginning. This small amount of energy input necessary for all chemical reactions to occur is called the **activation energy** (or free energy of activation) and is abbreviated E_A ([link](#)).

Why would an energy-releasing, negative ΔG reaction actually require some energy to proceed? The reason lies in the steps that take place during a chemical reaction. During chemical reactions, certain chemical bonds are

broken and new ones are formed. For example, when a glucose molecule is broken down, bonds between the carbon atoms of the molecule are broken. Since these are energy-storing bonds, they release energy when broken. However, to get them into a state that allows the bonds to break, the molecule must be somewhat contorted. A small energy input is required to achieve this contorted state. This contorted state is called the **transition state**, and it is a high-energy, unstable state. For this reason, reactant molecules don't last long in their transition state, but very quickly proceed to the next steps of the chemical reaction. Free energy diagrams illustrate the energy profiles for a given reaction. Whether the reaction is exergonic or endergonic determines whether the products in the diagram will exist at a lower or higher energy state than both the reactants and the products. However, regardless of this measure, the transition state of the reaction exists at a higher energy state than the reactants, and thus, E_A is always positive.

Note:

Link to Learning



Watch an animation of the move from free energy to transition state at [this](#) site.

Video Link

For a video to further explore activation energy click [here](#).

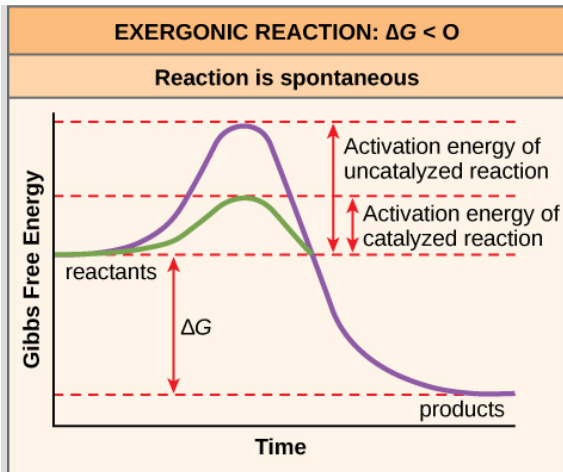
Where does the activation energy required by chemical reactants come from? The source of the activation energy needed to push reactions forward is typically heat energy from the surroundings. **Heat energy** (the total bond

energy of reactants or products in a chemical reaction) speeds up the motion of molecules, increasing the frequency and force with which they collide; it also moves atoms and bonds within the molecule slightly, helping them reach their transition state. For this reason, heating up a system will cause chemical reactants within that system to react more frequently. Increasing the pressure on a system has the same effect. Once reactants have absorbed enough heat energy from their surroundings to reach the transition state, the reaction will proceed.

The activation energy of a particular reaction determines the rate at which it will proceed. The higher the activation energy, the slower the chemical reaction will be. The example of iron rusting illustrates an inherently slow reaction. This reaction occurs slowly over time because of its high E_A . Additionally, the burning of many fuels, which is strongly exergonic, will take place at a negligible rate unless their activation energy is overcome by sufficient heat from a spark. Once they begin to burn, however, the chemical reactions release enough heat to continue the burning process, supplying the activation energy for surrounding fuel molecules. Like these reactions outside of cells, the activation energy for most cellular reactions is too high for heat energy to overcome at efficient rates. In other words, in order for important cellular reactions to occur at appreciable rates (number of reactions per unit time), their activation energies must be lowered ([\[link\]](#)); this is referred to as catalysis. This is a very good thing as far as living cells are concerned. Important macromolecules, such as proteins, DNA, and RNA, store considerable energy, and their breakdown is exergonic. If cellular temperatures alone provided enough heat energy for these exergonic reactions to overcome their activation barriers, the essential components of a cell would disintegrate.

Note:

Art Connection



Activation energy is the energy required for a reaction to proceed, and it is lower if the reaction is catalyzed. The horizontal axis of this diagram describes the sequence of events in time.

If no activation energy were required to break down sucrose (table sugar), would you be able to store it in a sugar bowl?

Exercise:

Activation Energy

Problem: Lowering the activation energy:

- makes the reaction happen faster
- lowers the energy level of the transition state
- is accomplished by adding a catalyst to the reaction
- always causes more product to be produced
- only reduces the transition state energy level in one direction, from reactants to products
- a, b and c
- b and c
- all of the above are true

Solution:

g

CONSERVATION OF ENERGY

Though energy can be converted from one form to another, energy cannot be created or destroyed. This principle is called the "law of conservation of energy." For example, in a motorcycle, the chemical potential energy of the fuel changes to kinetic energy. In a radio, electricity is converted into kinetic energy and wave energy (sound).

Machines can be used to convert energy from one form to another. Though ideal machines conserve the mechanical energy of a system, some of the energy always turns into heat when using a machine. For example, heat generated by friction is hard to collect and transform into another form of energy. In this situation, heat energy is usually considered unusable or lost.

Energy Sources

The source of energy for many processes occurring on the earth's surface comes from the sun. Radiating solar energy heats the earth unevenly, creating air movements in the atmosphere. Therefore, the sun drives the winds, ocean currents and the water cycle. Sunlight energy is used by plants to create chemical energy through a process called photosynthesis, and this supports the life and growth of plants. In addition, dead plant material decays, and over millions of years is converted into fossil fuels (oil, coal, etc.).

Today, we make use of various sources of energy found on earth to produce electricity. Using machines, we convert the energies of wind, biomass, fossil fuels, water, heat trapped in the earth (geothermal), nuclear and solar energy into usable electricity. The above sources of energy differ in amount,

availability, time required for their formation and usefulness. For example, the energy released by one gram of uranium during nuclear fission is much larger than that produced during the combustion of an equal mass of coal.

For this class, it is important for you to be able to identify the energy source for living cells. Whether we are discussing organisms such as trees or dogs, or individual cells, such as muscle or brain cells, or free living cells, such as bacteria or yeast, all cells need an energy source. Being able to identify the cellular energy source will be one of the goals of this class. In addition most metabolic reactions require an energy source as well. Identifying and applying these concepts will be a major focus of this course.

US ENERGY PRODUCTION (Quadrillion BTU)

(Source: US DOE)	1975	2000
Coal	14.989 (24.4%)	22.663 (31.5%)
Natural Gas (dry)	19.640 (32.0%)	19.741 (27.5%)
Crude Oil	17.729 (28.9%)	12.383 (17.2%)
Nuclear	1.900 (3.1%)	8.009 (11.2%)
Hydroelectric	3.155 (5.1%)	2.841 (4.0%)
Natural Gas (plant liquid)	2.374 (3.9%)	2.607 (3.6%)
Geothermal	0.070 (0.1%)	0.319 (0.4%)
Other	1.499 (2.5%)	3.275 (4.6%)
TOTAL	61.356	71.838

(Source: US Department of Energy)

What about energy in common biologically relevant molecules?

All cells require energy, without an energy supply cells quickly die. Shortly we will discuss in great detail how and where cells obtain energy. But first let's think about how much energy can be found in some common compounds associated with cells. We can get an idea by looking at the Enthalpy or Heat of Combustion (ΔH_c) which is the energy released as heat when a compound undergoes complete combustion with oxygen under standard conditions, of some common biologically relevant compounds.

Enthalpy of Combustion, ΔH_c

- Glucose ($C_6H_{12}O_6$) = -686 kcal/mol
- Methane (CH_4) = -215 kcal/mol
- Methanol (CH_3OH) = -144 kcal/mol
- Acetic acid ($C_2H_4O_2$) = -257 kcal/mol
- Hydrogen Sulfide (H_2S) = -134 kcal/mol
- Ammonia (NH_3) = -91.7 kcal/mol
- Hydrogen (H_2) = -68 kcal/mol
- Water (H_2O) = -17.2 kcal/mol
- CO_2 = -1.9 kcal/mol

Section Summary

Energy comes in many different forms. Objects in motion do physical work, and kinetic energy is the energy of objects in motion. Objects that are not in motion may have the potential to do work, and thus, have potential energy. Molecules also have potential energy because the breaking of molecular bonds has the potential to release energy. Living cells depend on the harvesting of potential energy from molecular bonds to perform work. Free energy is a measure of energy that is available to do work. The free energy

of a system changes during energy transfers such as chemical reactions, and this change is referred to as ΔG .

The ΔG of a reaction can be negative or positive, meaning that the reaction releases energy or consumes energy, respectively. A reaction with a negative ΔG that gives off energy is called an exergonic reaction. One with a positive ΔG that requires energy input is called an endergonic reaction. Exergonic reactions are said to be spontaneous, because their products have less energy than their reactants. The products of endergonic reactions have a higher energy state than the reactants, and so these are nonspontaneous reactions. However, all reactions (including spontaneous $-\Delta G$ reactions) require an initial input of energy in order to reach the transition state, at which they'll proceed. This initial input of energy is called the activation energy.

THERMODYNAMICS

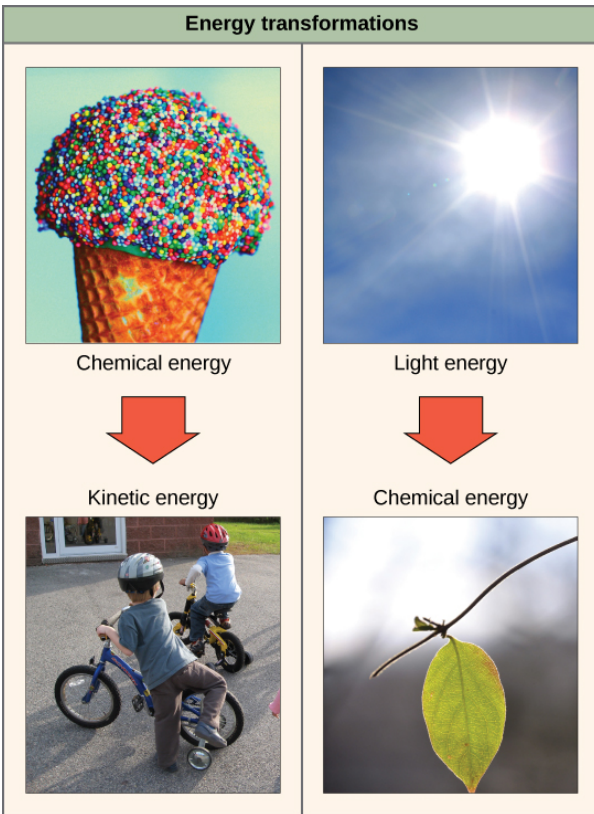
Thermodynamics refers to the study of energy and energy transfer involving physical matter. The matter and its environment relevant to a particular case of energy transfer are classified as a system, and everything outside of that system is called the surroundings. For instance, when heating a pot of water on the stove, the system includes the stove, the pot, and the water. Energy is transferred within the system (between the stove, pot, and water). There are two types of systems: open and closed. An open system is one in which energy can be transferred between the system and its surroundings. The stovetop system is open because heat can be lost into the air. A closed system is one that cannot transfer energy to its surroundings.

Biological organisms are open systems. Energy is exchanged between them and their surroundings, as they consume energy-storing molecules and release energy to the environment by doing work. Like all things in the physical world, energy is subject to the laws of physics. The laws of thermodynamics govern the transfer of energy in and among all systems in the universe.

The First Law of Thermodynamics

The first law of thermodynamics deals with the total amount of energy in the universe. It states that this total amount of energy is constant. In other words, there has always been, and always will be, exactly the same amount of energy in the universe. Energy exists in many different forms. According to the first law of thermodynamics, energy may be transferred from place to place or transformed into different forms, but it cannot be created or destroyed. The transfers and transformations of energy take place around us all the time. Light bulbs transform electrical energy into light energy. Gas stoves transform chemical energy from natural gas into heat energy. Plants perform one of the most biologically useful energy transformations on earth: that of converting the energy of sunlight into the chemical energy stored within organic molecules ([\[link\]](#)). Some examples of energy transformations are shown in [\[link\]](#).

The challenge for all living organisms is to obtain energy from their surroundings in forms that they can transfer or transform into usable energy to do work. Living cells have evolved to meet this challenge very well. Chemical energy stored within organic molecules such as sugars and fats is transformed through a series of cellular chemical reactions into energy within molecules of ATP. Energy in ATP molecules is easily accessible to do work. Examples of the types of work that cells need to do include building complex molecules, transporting materials, powering the beating motion of cilia or flagella, contracting muscle fibers to create movement, and reproduction.



Shown are two examples of energy being transferred from one system to another and transformed from one form to another. Humans can convert the chemical energy in food, like this ice cream cone, into kinetic energy (the energy of movement to ride a bicycle).

Plants can convert electromagnetic radiation (light energy) from the sun into chemical energy. (credit “ice cream”: modification of work by D. Sharon Pruitt; credit “kids on bikes”: modification of work by Michelle Riggen-Ransom;

credit “leaf”: modification of
work by Cory Zanker)

The Second Law of Thermodynamics

A living cell’s primary tasks of obtaining, transforming, and using energy to do work may seem simple. However, the second law of thermodynamics explains why these tasks are harder than they appear. None of the energy transfers we’ve discussed, along with all energy transfers and transformations in the universe, is completely efficient. In every energy transfer, some amount of energy is lost in a form that is unusable. In most cases, this form is heat energy. Thermodynamically, **heat energy** is defined as the energy transferred from one system to another that is not doing work. For example, when an airplane flies through the air, some of the energy of the flying plane is lost as heat energy due to friction with the surrounding air. This friction actually heats the air by temporarily increasing the speed of air molecules. Likewise, some energy is lost as heat energy during cellular metabolic reactions. This is good for warm-blooded creatures like us, because heat energy helps to maintain our body temperature. Strictly speaking, no energy transfer is completely efficient, because some energy is lost in an unusable form.

An important concept in physical systems is that of order and disorder (also known as randomness). The more energy that is lost by a system to its surroundings, the less ordered and more random the system is. Scientists refer to the measure of randomness or disorder within a system as **entropy**. High entropy means high disorder and low energy ([\[link\]](#)). To better understand entropy, think of a student’s bedroom. If no energy or work were put into it, the room would quickly become messy. It would exist in a very disordered state, one of high entropy. Energy must be put into the system, in the form of the student doing work and putting everything away, in order to bring the room back to a state of cleanliness and order. This state is one of low entropy. Similarly, a car or house must be constantly maintained with work in order to keep it in an ordered state. Left alone, the entropy of the

house or car gradually increases through rust and degradation. Molecules and chemical reactions have varying amounts of entropy as well. For example, as chemical reactions reach a state of equilibrium, entropy increases, and as molecules at a high concentration in one place diffuse and spread out, entropy also increases.

Note:

Scientific Connection

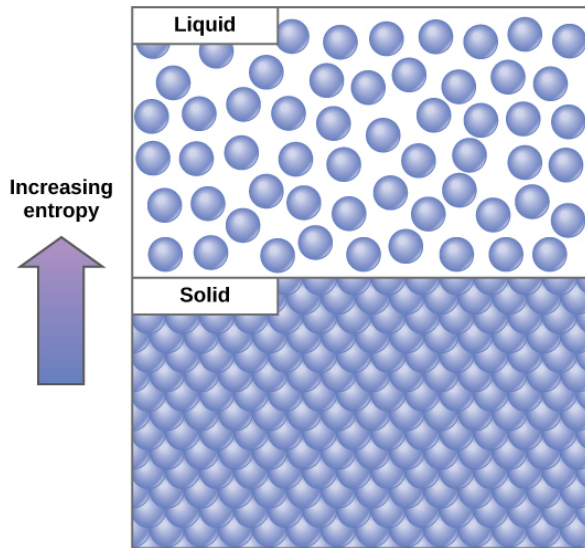
Transfer of Energy and the Resulting Entropy

Set up a simple experiment to understand how energy is transferred and how a change in entropy results.

1. Take a block of ice. This is water in solid form, so it has a high structural order. This means that the molecules cannot move very much and are in a fixed position. The temperature of the ice is 0°C . As a result, the entropy of the system is low.
2. Allow the ice to melt at room temperature. What is the state of molecules in the liquid water now? How did the energy transfer take place? Is the entropy of the system higher or lower? Why?
3. Heat the water to its boiling point. What happens to the entropy of the system when the water is heated?

All physical systems can be thought of in this way: Living things are highly ordered, requiring constant energy input to be maintained in a state of low entropy. As living systems take in energy-storing molecules and transform them through chemical reactions, they lose some amount of usable energy in the process, because no reaction is completely efficient. They also produce waste and by-products that aren't useful energy sources. This process increases the entropy of the system's surroundings. Since all energy transfers result in the loss of some usable energy, the second law of thermodynamics states that every energy transfer or transformation increases the entropy of the universe. Even though living things are highly ordered and maintain a state of low entropy, the entropy of the universe in

total is constantly increasing due to the loss of usable energy with each energy transfer that occurs. Essentially, living things are in a continuous uphill battle against this constant increase in universal entropy.



Entropy is a measure of randomness or disorder in a system. Gases have higher entropy than liquids, and liquids have higher entropy than solids.

Section Summary

In studying energy, scientists use the term “system” to refer to the matter and its environment involved in energy transfers. Everything outside of the system is called the surroundings. Single cells are biological systems. Systems can be thought of as having a certain amount of order. It takes energy to make a system more ordered. The more ordered a system is, the lower its entropy. Entropy is a measure of the disorder of a system. As a

system becomes more disordered, the lower its energy and the higher its entropy become.

A series of laws, called the laws of thermodynamics, describe the properties and processes of energy transfer. The first law states that the total amount of energy in the universe is constant. This means that energy can't be created or destroyed, only transferred or transformed. The second law of thermodynamics states that every energy transfer involves some loss of energy in an unusable form, such as heat energy, resulting in a more disordered system. In other words, no energy transfer is completely efficient and tends toward disorder.

Summary Review Questions

Exercise:

Problem:

[\[link\]](#) Look at each of the processes shown, and decide if it is endergonic or exergonic. In each case, does enthalpy increase or decrease, and does entropy increase or decrease?

Solution:

[\[link\]](#) A compost pile decomposing is an exergonic process; enthalpy increases (energy is released) and entropy increases (large molecules are broken down into smaller ones). A baby developing from a fertilized egg is an endergonic process; enthalpy decreases (energy is absorbed) and entropy decreases. Sand art being destroyed is an exergonic process; there is no change in enthalpy, but entropy increases. A ball rolling downhill is an exergonic process; enthalpy decreases (energy is released), but there is no change in enthalpy.

Exercise:

Problem:

[\[link\]](#) If no activation energy were required to break down sucrose (table sugar), would you be able to store it in a sugar bowl?

Solution:

[\[link\]](#) No. We can store chemical energy because of the need to overcome the barrier to its breakdown.

Exercise:**Problem:**

Consider a pendulum swinging. Which type(s) of energy is/are associated with the pendulum in the following instances: i. the moment at which it completes one cycle, just before it begins to fall back towards the other end, ii. the moment that it is in the middle between the two ends, iii. just before it reaches the end of one cycle (just before instant i.).

- a. i. potential and kinetic, ii. potential and kinetic, iii. kinetic
 - b. i. potential, ii. potential and kinetic, iii. potential and kinetic
 - c. i. potential, ii. kinetic, iii. potential and kinetic
 - d. i. potential and kinetic, ii. kinetic iii. kinetic
-

Solution:

C

Exercise:**Problem:**

Which of the following comparisons or contrasts between endergonic and exergonic reactions is false?

- a. Endergonic reactions have a positive ΔG and exergonic reactions have a negative ΔG
 - b. Endergonic reactions consume energy and exergonic reactions release energy
 - c. Both endergonic and exergonic reactions require a small amount of energy to overcome an activation barrier
 - d. Endergonic reactions take place slowly and exergonic reactions take place quickly
-

Solution:

D

Exercise:

Problem:

Which of the following is the best way to judge the relative activation energies between two given chemical reactions?

- a. Compare the ΔG values between the two reactions
 - b. Compare their reaction rates
 - c. Compare their ideal environmental conditions
 - d. Compare the spontaneity between the two reactions
-

Solution:

B

Exercise:

Problem:

Explain in your own words the difference between a spontaneous reaction and one that occurs instantaneously, and what causes this difference.

Solution:

A spontaneous reaction is one that has a negative ΔG and thus releases energy. However, a spontaneous reaction need not occur quickly or suddenly like an instantaneous reaction. It may occur over long periods due to a large energy of activation, which prevents the reaction from occurring quickly.

Exercise:**Problem:**

Describe the position of the transition state on a vertical energy scale, from low to high, relative to the position of the reactants and products, for both endergonic and exergonic reactions.

Solution:

The transition state is always higher in energy than the reactants and the products of a reaction (therefore, above), regardless of whether the reaction is endergonic or exergonic.

Exercise:**Problem:**

Which of the following is not an example of an energy transformation?

- a. Turning on a light switch
- b. Solar panels at work
- c. Formation of static electricity
- d. None of the above

Solution:

A

Exercise:**Problem:**

Label each of the following systems as high or low entropy: i. the instant that a perfume bottle is sprayed compared with 30 seconds later, ii. an old 1950s car compared with a brand new car, and iii. a living cell compared with a dead cell.

- a. i. low, ii. high, iii. low
- b. i. low, ii. high, iii. high
- c. i. high, ii. low, iii. high
- d. i. high, ii. low, iii. Low

Solution:

A

Exercise:**Problem:**

Imagine an elaborate ant farm with tunnels and passageways through the sand where ants live in a large community. Now imagine that an earthquake shook the ground and demolished the ant farm. In which of these two scenarios, before or after the earthquake, was the ant farm system in a state of higher or lower entropy?

Solution:

The ant farm had lower entropy before the earthquake because it was a highly ordered system. After the earthquake, the system became much more disordered and had higher entropy.

Exercise:

Problem:

Energy transfers take place constantly in everyday activities. Think of two scenarios: cooking on a stove and driving. Explain how the second law of thermodynamics applies to these two scenarios.

Solution:

While cooking, food is heating up on the stove, but not all of the heat goes to cooking the food, some of it is lost as heat energy to the surrounding air, increasing entropy. While driving, cars burn gasoline to run the engine and move the car. This reaction is not completely efficient, as some energy during this process is lost as heat energy, which is why the hood and the components underneath it heat up while the engine is turned on. The tires also heat up because of friction with the pavement, which is additional energy loss. This energy transfer, like all others, also increases entropy.

Appendix I: Energy Units

In the International System of Units (SI), the unit of work or energy is the **Joule (J)**. For very small amounts of energy, the erg (erg) is sometimes used. An **erg** is one ten millionth of a Joule:

Equation:

$$1 \text{ Joule} = 10,000,000 \text{ ergs}$$

Power is the rate at which energy is used. The unit of power is the **Watt (W)**, named after James Watt, who perfected the steam engine:

Equation:

$$1 \text{ Watt} = 1 \text{ Joule/second}$$

Power is sometimes measured in **horsepower (hp)**:

Equation:

$$1 \text{ horsepower} = 746 \text{ Watts}$$

Electrical energy is generally expressed in **kilowatt-hours (kWh)**:

Equation:

$$1 \text{ kilowatt} - \text{hour} = 3,600,000 \text{ Joules}$$

It is important to realize that a kilowatt-hour is a unit of energy not power. For example, an iron rated at 2000 Watts would consume $2 \times 3.6 \times 10^6 \text{ J}$ of energy in 1 hour .

Heat energy is often measured in calories. One calorie (cal) is defined as the heat required to raise the temperature of 1 gram of water from 14.5 to 15.5 °C:

Equation:

$$1 \text{ calorie} = 4.189 \text{ Joules}$$

An old, but still used unit of heat is the **British Thermal Unit (BTU)**. It is defined as the heat energy required to raise the energy temperature of 1 pound of water from 63 to 64 °F.

$$1 \text{ BTU} = 1055 \text{ Joules}$$

Physical Quantity	Name	Symbol	SI Unit
Force	Newton	N	$\text{kg} \cdot \text{m}/\text{s}^2$
Energy	Joule	J	$\text{kg} \cdot \text{m}^2/\text{s}^2$

Power	Watt	W	$\text{kg} \cdot \text{m}^2/\text{s}^3$
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Glossary

activation energy

energy necessary for reactions to occur

chemical energy

potential energy in chemical bonds that is released when those bonds are broken

endergonic

describes chemical reactions that require energy input

enthalpy

total energy of a system

exergonic

describes chemical reactions that release free energy

free energy

Gibbs free energy is the usable energy, or energy that is available to do work.

heat energy

total bond energy of reactants or products in a chemical reaction

kinetic energy

type of energy associated with objects or particles in motion

potential energy

type of energy that has the potential to do work; stored energy

transition state

high-energy, unstable state (an intermediate form between the substrate and the product) occurring during a chemical reaction

Bis2A 05.0 Introduction Biological reactions and catalysts

class="introduction"

A hummingbird needs energy to maintain prolonged periods of flight. The bird obtains its energy from taking in food and transforming the nutrients into energy through a series of biochemical reactions. The flight muscles in birds are extremely efficient in energy production. (credit: modification of work by Cory Zanker)



Virtually every task performed by living organisms requires energy. Energy is needed to perform heavy labor and exercise, but humans also use a great deal of energy while thinking, and even during sleep. In fact, the living cells of every organism constantly use energy. Nutrients and other molecules are imported, metabolized (broken down) and possibly synthesized into new molecules, modified if needed, transported around the cell, and may be distributed to the entire organism. For example, the large proteins that make up muscles are actively built from smaller molecules. Complex carbohydrates are broken down into simple sugars that the cell uses for energy. Just as energy is required to both build and demolish a building, energy is required for both the synthesis and breakdown of molecules. Additionally, signaling molecules such as hormones and neurotransmitters are transported between cells. Pathogenic bacteria and viruses are ingested and broken down by cells. Cells must also export waste and toxins to stay healthy, and many cells must swim or move surrounding materials via the beating motion of cellular appendages like cilia and flagella.

The cellular processes listed above require a steady supply of energy. From where, and in what form, does this energy come? How do living cells obtain energy, and how do they use it? This chapter will discuss different forms of energy and the physical laws that govern energy transfer. This chapter will

also describe how cells use energy and replenish it, and how chemical reactions in the cell are performed with great efficiency.

Bis2A 05.1 Chemical Reactions

By the end of this section, you will be able to:

- Distinguish between kinetic and potential energy, and between exergonic and endergonic chemical reactions
- Identify four forms of energy important in human functioning
- Describe the three basic types of chemical reactions
- Identify several factors influencing the rate of chemical reactions

One characteristic of a living organism is metabolism, which is the sum total of all of the chemical reactions that go on to maintain that organism's health and life. The bonding processes you have learned thus far are anabolic chemical reactions; that is, they form larger molecules from smaller molecules or atoms. But recall that metabolism can proceed in another direction: in catabolic chemical reactions, bonds between components of larger molecules break, releasing smaller molecules or atoms. Both types of reaction involve exchanges not only of matter, but of energy.

The Role of Energy in Chemical Reactions

Chemical reactions require a sufficient amount of energy to cause the matter to collide with enough precision and force that old chemical bonds can be broken and new ones formed. In general, **kinetic energy** is the form of energy powering any type of matter in motion. Imagine you are building a brick wall. The energy it takes to lift and place one brick atop another is kinetic energy—the energy matter possesses because of its motion. Once the wall is in place, it stores potential energy. **Potential energy** is the energy of position, or the energy matter possesses because of the positioning or structure of its components. If the brick wall collapses, the stored potential energy is released as kinetic energy as the bricks fall.

In the human body, potential energy is stored in the bonds between atoms and molecules. **Chemical energy** is the form of potential energy in which energy is stored in chemical bonds. When those bonds are formed, chemical energy is invested, and when they break, chemical energy is released. Notice that chemical energy, like all energy, is neither created nor

destroyed; rather, it is converted from one form to another. When you eat an energy bar before heading out the door for a hike, the honey, nuts, and other foods the bar contains are broken down and rearranged by your body into molecules that your muscle cells convert to kinetic energy.

Chemical reactions that release more energy than they absorb are characterized as exergonic. The catabolism of the foods in your energy bar is an example. Some of the chemical energy stored in the bar is absorbed into molecules your body uses for fuel, but some of it is released—for example, as heat. In contrast, chemical reactions that absorb more energy than they release are endergonic. These reactions require energy input, and the resulting molecule stores not only the chemical energy in the original components, but also the energy that fueled the reaction. Because energy is neither created nor destroyed, where does the energy needed for endergonic reactions come from? In many cases, it comes from exergonic reactions.

Forms of Energy Important in Human Functioning

You have already learned that chemical energy is absorbed, stored, and released by chemical bonds. In addition to chemical energy, mechanical, radiant, and electrical energy are important in human functioning.

- Mechanical energy, which is stored in physical systems such as machines, engines, or the human body, directly powers the movement of matter. When you lift a brick into place on a wall, your muscles provide the mechanical energy that moves the brick.
- Radiant energy is energy emitted and transmitted as waves rather than matter. These waves vary in length from long radio waves and microwaves to short gamma waves emitted from decaying atomic nuclei. The full spectrum of radiant energy is referred to as the electromagnetic spectrum. The body uses the ultraviolet energy of sunlight to convert a compound in skin cells to vitamin D, which is essential to human functioning. The human eye evolved to see the wavelengths that comprise the colors of the rainbow, from red to violet, so that range in the spectrum is called “visible light.”
- Electrical energy, supplied by electrolytes in cells and body fluids, contributes to the voltage changes that help transmit impulses in nerve

and muscle cells.

Characteristics of Chemical Reactions

All chemical reactions begin with a **reactant**, the general term for the one or more substances that enter into the reaction. Sodium and chloride ions, for example, are the reactants in the production of table salt. The one or more substances produced by a chemical reaction are called the **product**.

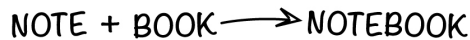
In chemical reactions, the components of the reactants—the elements involved and the number of atoms of each—are all present in the product(s). Similarly, there is nothing present in the products that are not present in the reactants. This is because chemical reactions are governed by the law of conservation of mass, which states that matter cannot be created or destroyed in a chemical reaction.

Just as you can express mathematical calculations in equations such as $2 + 7 = 9$, you can use chemical equations to show how reactants become products. As in math, chemical equations proceed from left to right, but instead of an equal sign, they employ an arrow or arrows indicating the direction in which the chemical reaction proceeds. For example, the chemical reaction in which one atom of nitrogen and three atoms of hydrogen produce ammonia would be written as $\text{N} + 3\text{H} \rightarrow \text{NH}_3$. Correspondingly, the breakdown of ammonia into its components would be written as $\text{NH}_3 \rightarrow \text{N} + 3\text{H}$.

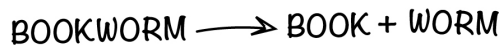
Notice that, in the first example, a nitrogen (N) atom and three hydrogen (H) atoms bond to form a compound. This anabolic reaction requires energy, which is then stored within the compound's bonds. Such reactions are referred to as synthesis reactions. A **synthesis reaction** is a chemical reaction that results in the synthesis (joining) of components that were formerly separate ([link](#)). Again, nitrogen and hydrogen are reactants in a synthesis reaction that yields ammonia as the product. The general equation for a synthesis reaction is $\text{A} + \text{B} \rightarrow \text{AB}$.

The Three Fundamental Chemical Reactions

a) In a synthesis reaction, two components bond to make a larger molecule. Energy is required and is stored in the bond:



b) In a decomposition reaction, bonds between components of a larger molecule are broken, resulting in smaller products:



c) In an exchange reaction, bonds are both formed and broken such that the components of the reactants are rearranged:



The atoms and molecules involved in the three fundamental chemical reactions can be imagined as words.

In the second example, ammonia is catabolized into its smaller components, and the potential energy that had been stored in its bonds is released. Such reactions are referred to as decomposition reactions. A **decomposition reaction** is a chemical reaction that breaks down or “de-composes” something larger into its constituent parts (see [\[link\]b](#)). The general equation for a decomposition reaction is: $AB \rightarrow A + B$.

An **exchange reaction** is a chemical reaction in which both synthesis and decomposition occur, chemical bonds are both formed and broken, and chemical energy is absorbed, stored, and released (see [\[link\]c](#)). The simplest form of an exchange reaction might be: $A + BC \rightarrow AB + C$. Notice that, to produce these products, B and C had to break apart in a decomposition reaction, whereas A and B had to bond in a synthesis reaction. A more complex exchange reaction might be: $AB + CD \rightarrow AC + BD$. Another example might be: $AB + CD \rightarrow AD + BC$.

In theory, any chemical reaction can proceed in either direction under the right conditions. Reactants may synthesize into a product that is later decomposed. Reversibility is also a quality of exchange reactions. For instance, $A + BC \rightarrow AB + C$ could then reverse to $AB + C \rightarrow A + BC$. This reversibility of a chemical reaction is indicated with a double arrow: $A + BC \rightleftharpoons AB + C$. Still, in the human body, many chemical reactions do

proceed in a predictable direction, either one way or the other. You can think of this more predictable path as the path of least resistance because, typically, the alternate direction requires more energy.

Factors Influencing the Rate of Chemical Reactions

If you pour vinegar into baking soda, the reaction is instantaneous; the concoction will bubble and fizz. But many chemical reactions take time. A variety of factors influence the rate of chemical reactions. This section, however, will consider only the most important in human functioning.

Properties of the Reactants

If chemical reactions are to occur quickly, the atoms in the reactants have to have easy access to one another. Thus, the greater the surface area of the reactants, the more readily they will interact. When you pop a cube of cheese into your mouth, you chew it before you swallow it. Among other things, chewing increases the surface area of the food so that digestive chemicals can more easily get at it. As a general rule, gases tend to react faster than liquids or solids, again because it takes energy to separate particles of a substance, and gases by definition already have space between their particles. Similarly, the larger the molecule, the greater the number of total bonds, so reactions involving smaller molecules, with fewer total bonds, would be expected to proceed faster.

In addition, recall that some elements are more reactive than others. Reactions that involve highly reactive elements like hydrogen proceed more quickly than reactions that involve less reactive elements. Reactions involving stable elements like helium are not likely to happen at all.

Video Link

So, how can you speed up chemical reaction? For an over view check out the following short (4 minute) video on chemical reactions by clicking [here](#).

Temperature

Nearly all chemical reactions occur at a faster rate at higher temperatures. Recall that kinetic energy is the energy of matter in motion. The kinetic energy of subatomic particles increases in response to increases in thermal energy. The higher the temperature, the faster the particles move, and the more likely they are to come in contact and react.

Concentration and Pressure

If just a few people are dancing at a club, they are unlikely to step on each other's toes. But as more and more people get up to dance—especially if the music is fast—collisions are likely to occur. It is the same with chemical reactions: the more particles present within a given space, the more likely those particles are to bump into one another. This means that chemists can speed up chemical reactions not only by increasing the **concentration** of particles—the number of particles in the space—but also by decreasing the volume of the space, which would correspondingly increase the pressure. If there were 100 dancers in that club, and the manager abruptly moved the party to a room half the size, the concentration of the dancers would double in the new space, and the likelihood of collisions would increase accordingly.

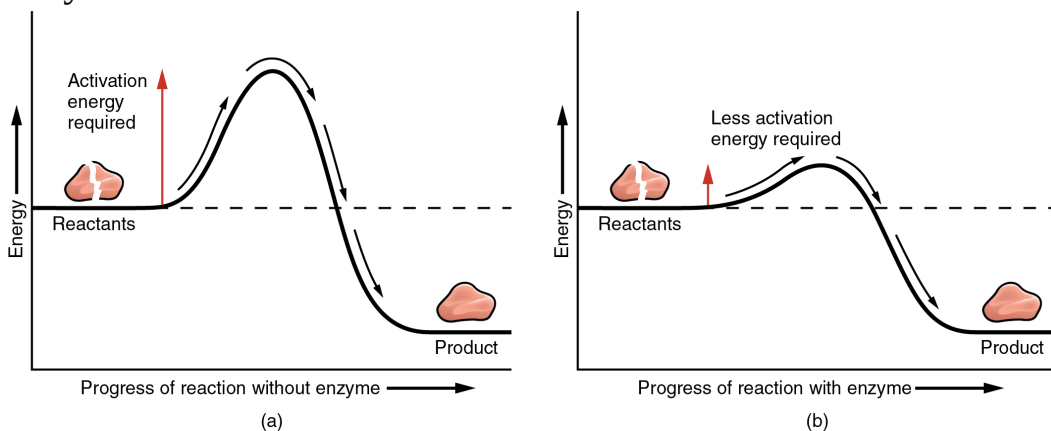
Enzymes and Other Catalysts

For two chemicals in nature to react with each other they first have to come into contact, and this occurs through random collisions. Because heat helps increase the kinetic energy of atoms, ions, and molecules, it promotes their collision. But in the body, extremely high heat—such as a very high fever—can damage body cells and be life-threatening. On the other hand, normal body temperature is not high enough to promote the chemical reactions that sustain life. That is where catalysts come in.

In chemistry, a **catalyst** is a substance that increases the rate of a chemical reaction without itself undergoing any change. You can think of a catalyst as a chemical change agent. They help increase the rate and force at which atoms, ions, and molecules collide, thereby increasing the probability that their valence shell electrons will interact.

The most important catalysts in the human body are enzymes. An **enzyme** is a catalyst composed of protein or ribonucleic acid (RNA), both of which will be discussed later in this chapter. Like all catalysts, enzymes work by lowering the level of energy that needs to be invested in a chemical reaction. A chemical reaction's **activation energy** is the “threshold” level of energy needed to break the bonds in the reactants. Once those bonds are broken, new arrangements can form. Without an enzyme to act as a catalyst, a much larger investment of energy is needed to ignite a chemical reaction ([\[link\]](#)).

Enzymes



Enzymes decrease the activation energy required for a given chemical reaction to occur. (a) Without an enzyme, the energy input needed for a reaction to begin is high. (b) With the help of an enzyme, less energy is needed for a reaction to begin.

Enzymes are critical to the body's healthy functioning. They assist, for example, with the breakdown of food and its conversion to energy. In fact, most of the chemical reactions in the body are facilitated by enzymes.

Summary

Chemical reactions, in which chemical bonds are broken and formed, require an initial investment of energy. Kinetic energy, the energy of matter in motion, fuels the collisions of atoms, ions, and molecules that are necessary if their old bonds are to break and new ones to form. All molecules store potential energy, which is released when their bonds are broken.

Four forms of energy essential to human functioning are: chemical energy, which is stored and released as chemical bonds are formed and broken; mechanical energy, which directly powers physical activity; radiant energy, emitted as waves such as in sunlight; and electrical energy, the power of moving electrons.

Chemical reactions begin with reactants and end with products. Synthesis reactions bond reactants together, a process that requires energy, whereas decomposition reactions break the bonds within a reactant and thereby release energy. In exchange reactions, bonds are both broken and formed, and energy is exchanged.

The rate at which chemical reactions occur is influenced by several properties of the reactants: temperature, concentration and pressure, and the presence or absence of a catalyst. An enzyme is a catalytic protein that speeds up chemical reactions in the human body.

Review Questions

Exercise:

Problem:

The energy stored in a foot of snow on a steep roof is _____.

- a. potential energy
- b. kinetic energy
- c. radiant energy
- d. activation energy

Solution:

A

Exercise:

Problem:

The bonding of calcium, phosphorus, and other elements produces mineral crystals that are found in bone. This is an example of a(n) _____ reaction.

- a. catabolic
- b. synthesis
- c. decomposition
- d. exchange

Solution:

B

Exercise:

Problem:

$AB \rightarrow A + B$ is a general notation for a(n) _____ reaction.

- a. anabolic
- b. endergonic
- c. decomposition
- d. exchange

Solution:

C

Exercise:

Problem:_____ reactions release energy.

- a. Catabolic
- b. Exergonic
- c. Decomposition
- d. Catabolic, exergonic, and decomposition

Solution:

D

Exercise:

Problem:

Which of the following combinations of atoms is *most likely* to result in a chemical reaction?

- a. hydrogen and hydrogen
- b. hydrogen and helium
- c. helium and helium
- d. neon and helium

Solution:

A

Exercise:

Problem:

Chewing a bite of bread mixes it with saliva and facilitates its chemical breakdown. This is *most likely* due to the fact that _____.

- a. the inside of the mouth maintains a very high temperature
- b. chewing stores potential energy
- c. chewing facilitates synthesis reactions

d. saliva contains enzymes

Solution:

D

Critical Thinking Questions

Exercise:

Problem:

$AB + CD \rightarrow AD + BE$ Is this a legitimate example of an exchange reaction? Why or why not?

Solution:

It is not. An exchange reaction might be $AB + CD \rightarrow AC + BD$ or $AB + CD \rightarrow AD + BC$. In all chemical reactions, including exchange reactions, the components of the reactants are identical to the components of the products. A component present among the reactants cannot disappear, nor can a component not present in the reactants suddenly appear in the products.

Exercise:

Problem:

When you do a load of laundry, why do you not just drop a bar of soap into the washing machine? In other words, why is laundry detergent sold as a liquid or powder?

Solution:

Recall that the greater the surface area of the reactants, the more quickly and easily they will interact. It takes energy to separate particles of a substance. Powder and liquid laundry detergents, with

relatively more surface area per unit, can quickly dissolve into their reactive components when added to the water.

Glossary

activation energy

amount of energy greater than the energy contained in the reactants, which must be overcome for a reaction to proceed

catalyst

substance that increases the rate of a chemical reaction without itself being changed in the process

chemical energy

form of energy that is absorbed as chemical bonds form, stored as they are maintained, and released as they are broken

concentration

number of particles within a given space

decomposition reaction

type of catabolic reaction in which one or more bonds within a larger molecule are broken, resulting in the release of smaller molecules or atoms

enzyme

protein or RNA that catalyzes chemical reactions

exchange reaction

type of chemical reaction in which bonds are both formed and broken, resulting in the transfer of components

kinetic energy

energy that matter possesses because of its motion

potential energy

stored energy matter possesses because of the positioning or structure of its components

product

one or more substances produced by a chemical reaction

reactant

one or more substances that enter into the reaction

synthesis reaction

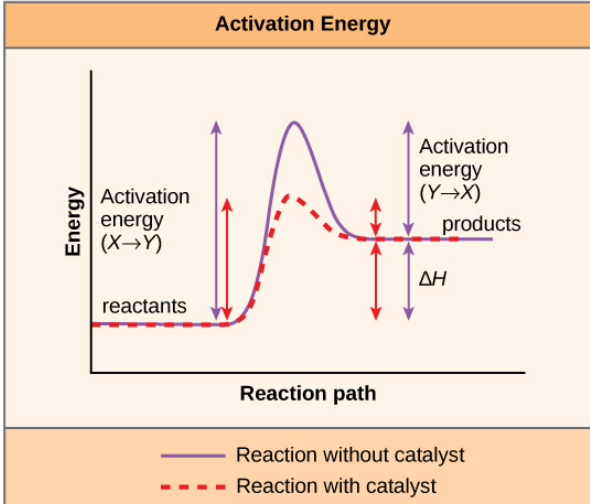
type of anabolic reaction in which two or more atoms or molecules bond, resulting in the formation of a larger molecule

Bis2A 05.2 Enzymes

By the end of this section, you will be able to:

- Describe the role of enzymes in metabolic pathways
- Explain how enzymes function as molecular catalysts
- Discuss enzyme regulation by various factors

A substance that helps a chemical reaction to occur is a **catalyst**, and the special molecules that catalyze biochemical reactions are called **enzymes**. Almost all enzymes are proteins, made up of chains of amino acids, and they perform the critical task of lowering the activation energies of chemical reactions inside the cell. Enzymes do this by binding to the reactant molecules, and holding them in such a way as to make the chemical bond-breaking and bond-forming processes take place more readily. It is important to remember that enzymes don't change the ΔG of a reaction. In other words, they don't change whether a reaction is exergonic (spontaneous) or endergonic. This is because they don't change the free energy of the reactants or products. They only reduce the activation energy required to reach the transition state ([\[link\]](#)).



Enzymes lower the activation energy of the reaction but do not change the free energy of the reaction.

Enzyme Active Site and Substrate Specificity

The chemical reactants to which an enzyme binds are the enzyme's **substrates**. There may be one or more substrates, depending on the particular chemical reaction. In some reactions, a single-reactant substrate is broken down into multiple products. In others, two substrates may come together to create one larger molecule. Two reactants might also enter a reaction, both become modified, and leave the reaction as two products. The location within the enzyme where the substrate binds is called the enzyme's **active site**. The active site is where the "action" happens, so to speak. Since enzymes are proteins, there is a unique combination of amino acid residues (also called side chains, or R groups) within the active site. Each residue is characterized by different properties. Residues can be large or small, weakly acidic or basic, hydrophilic or hydrophobic, positively or negatively charged, or neutral. The unique combination of amino acid residues, their positions, sequences, structures, and properties, creates a very specific chemical environment within the active site. This specific environment is suited to bind, albeit briefly, to a specific chemical substrate (or substrates). Due to this jigsaw puzzle-like match between an enzyme and its substrates (which adapts to find the best fit between the transition state and the active site), enzymes are known for their specificity. The "best fit" results from the shape and the amino acid functional group's attraction to the substrate. There is a specifically matched enzyme for each substrate and, thus, for each chemical reaction; however, there is flexibility as well.

The fact that active sites are so perfectly suited to provide specific environmental conditions also means that they are subject to influences by the local environment. It is true that increasing the environmental temperature generally increases reaction rates, enzyme-catalyzed or otherwise. However, increasing or decreasing the temperature outside of an optimal range can affect chemical bonds within the active site in such a way that they are less well suited to bind substrates. High temperatures will eventually cause enzymes, like other biological molecules, to **denature**, a process that changes the natural properties of a substance. Likewise, the pH of the local environment can also affect enzyme function. Active site amino acid residues have their own acidic or basic properties that are optimal for catalysis. These residues are sensitive to changes in pH that can impair the

way substrate molecules bind. Enzymes are suited to function best within a certain pH range, and, as with temperature, extreme pH values (acidic or basic) of the environment can cause enzymes to denature.

Induced Fit and Enzyme Function

For many years, scientists thought that enzyme-substrate binding took place in a simple “lock-and-key” fashion. This model asserted that the enzyme and substrate fit together perfectly in one instantaneous step. However, current research supports a more refined view called **induced fit** ([link](#)). The induced-fit model expands upon the lock-and-key model by describing a more dynamic interaction between enzyme and substrate. As the enzyme and substrate come together, their interaction causes a mild shift in the enzyme’s structure that confirms an ideal binding arrangement between the enzyme and the transition state of the substrate. This ideal binding maximizes the enzyme’s ability to catalyze its reaction.

Note:

Link to Learning



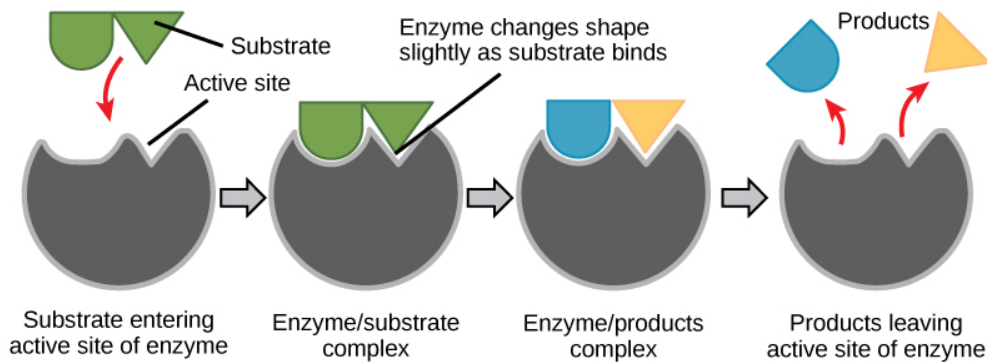
View an animation of induced fit at [this website](#).

Video Link

Here is another short video (2 minutes) from the University of Surrey on enzyme-substrate interactions. Click [here](#) for the video.

When an enzyme binds its substrate, an enzyme-substrate complex is formed. This complex lowers the activation energy of the reaction and promotes its rapid progression in one of many ways. On a basic level, enzymes promote chemical reactions that involve more than one substrate by bringing the substrates together in an optimal orientation. The appropriate region (atoms and bonds) of one molecule is juxtaposed to the appropriate region of the other molecule with which it must react. Another way in which enzymes promote the reaction of their substrates is by creating an optimal environment within the active site for the reaction to occur. Certain chemical reactions might proceed best in a slightly acidic or non-polar environment. The chemical properties that emerge from the particular arrangement of amino acid residues within an active site create the perfect environment for an enzyme's specific substrates to react.

You've learned that the activation energy required for many reactions includes the energy involved in manipulating or slightly contorting chemical bonds so that they can easily break and allow others to reform. Enzymatic action can aid this process. The enzyme-substrate complex can lower the activation energy by contorting substrate molecules in such a way as to facilitate bond-breaking, helping to reach the transition state. Finally, enzymes can also lower activation energies by taking part in the chemical reaction itself. The amino acid residues can provide certain ions or chemical groups that actually form covalent bonds with substrate molecules as a necessary step of the reaction process. In these cases, it is important to remember that the enzyme will always return to its original state at the completion of the reaction. One of the hallmark properties of enzymes is that they remain ultimately unchanged by the reactions they catalyze. After an enzyme is done catalyzing a reaction, it releases its product(s).



According to the induced-fit model, both enzyme and substrate undergo dynamic conformational changes upon binding. The enzyme contorts the substrate into its transition state, thereby increasing the rate of the reaction.

Control of Metabolism Through Enzyme Regulation

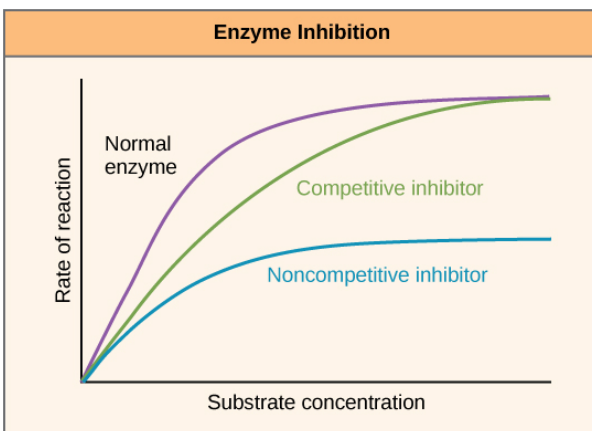
It would seem ideal to have a scenario in which all of the enzymes encoded in an organism's genome existed in abundant supply and functioned optimally under all cellular conditions, in all cells, at all times. In reality, this is far from the case. A variety of mechanisms ensure that this does not happen. Cellular needs and conditions vary from cell to cell, and change within individual cells over time. The required enzymes and energetic demands of stomach cells are different from those of fat storage cells, skin cells, blood cells, and nerve cells. Furthermore, a digestive cell works much harder to process and break down nutrients during the time that closely follows a meal compared with many hours after a meal. As these cellular demands and conditions vary, so do the amounts and functionality of different enzymes.

Since the rates of biochemical reactions are controlled by activation energy, and enzymes lower and determine activation energies for chemical reactions, the relative amounts and functioning of the variety of enzymes within a cell ultimately determine which reactions will proceed and at

which rates. This determination is tightly controlled. In certain cellular environments, enzyme activity is partly controlled by environmental factors, like pH and temperature. There are other mechanisms through which cells control the activity of enzymes and determine the rates at which various biochemical reactions will occur.

Regulation of Enzymes by Molecules

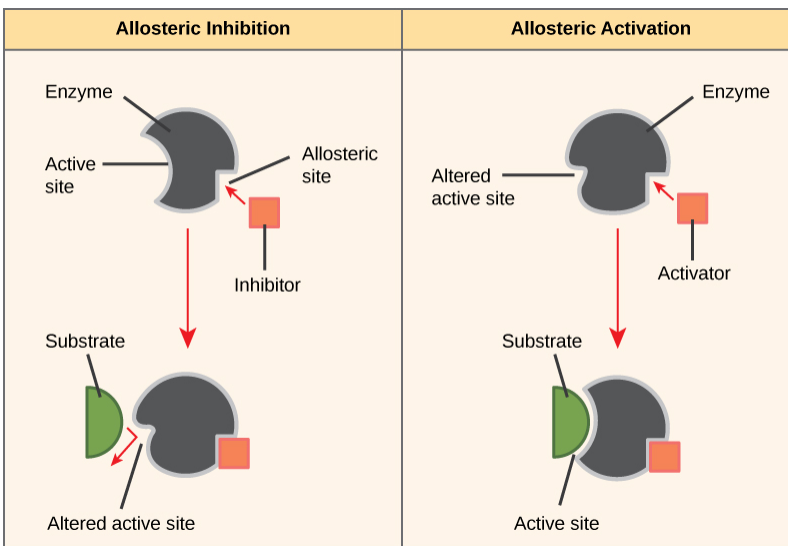
Enzymes can be regulated in ways that either promote or reduce their activity. There are many different kinds of molecules that inhibit or promote enzyme function, and various mechanisms exist for doing so. In some cases of enzyme inhibition, for example, an inhibitor molecule is similar enough to a substrate that it can bind to the active site and simply block the substrate from binding. When this happens, the enzyme is inhibited through **competitive inhibition**, because an inhibitor molecule competes with the substrate for active site binding ([link](#)). On the other hand, in noncompetitive inhibition, an inhibitor molecule binds to the enzyme in a location other than an allosteric site and still manages to block substrate binding to the active site.



Competitive and noncompetitive inhibition affect the rate of reaction differently. Competitive inhibitors affect

the initial rate but do not affect the maximal rate, whereas noncompetitive inhibitors affect the maximal rate.

Some inhibitor molecules bind to enzymes in a location where their binding induces a conformational change that reduces the affinity of the enzyme for its substrate. This type of inhibition is called **allosteric inhibition** ([\[link\]](#)). Most allosterically regulated enzymes are made up of more than one polypeptide, meaning that they have more than one protein subunit. When an allosteric inhibitor binds to an enzyme, all active sites on the protein subunits are changed slightly such that they bind their substrates with less efficiency. There are **allosteric activators** as well as inhibitors. Allosteric activators bind to locations on an enzyme away from the active site, inducing a conformational change that increases the affinity of the enzyme's active site(s) for its substrate(s).



Allosteric inhibitors modify the active site of the enzyme so that substrate binding is reduced or prevented. In contrast, allosteric activators modify the active site of the

enzyme so that the affinity for the substrate increases.

Video Link

Check out this short (1 minute) video on [competitive vs. noncompetitive](#) enzymatic inhibition. Also, take a look at this video (1.2 minutes) on [feed back inhibition](#).

Note:

Everyday Connection



Have you ever wondered how pharmaceutical drugs are developed? (credit: Deborah Austin)

Drug Discovery by Looking for Inhibitors of Key Enzymes in Specific Pathways

Enzymes are key components of metabolic pathways. Understanding how enzymes work and how they can be regulated is a key principle behind the development of many of the pharmaceutical drugs ([\[link\]](#)) on the market

today. Biologists working in this field collaborate with other scientists, usually chemists, to design drugs.

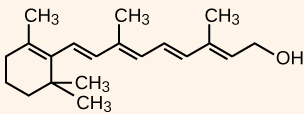
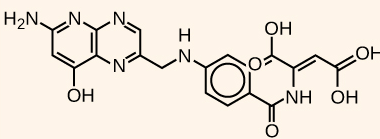
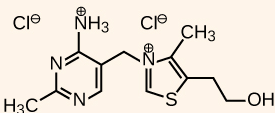
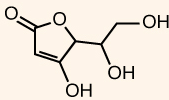
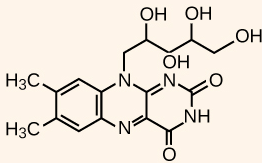
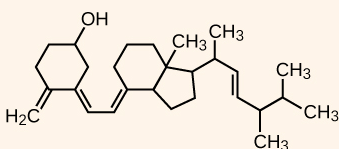
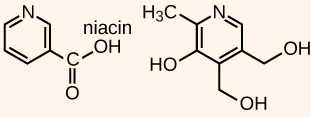
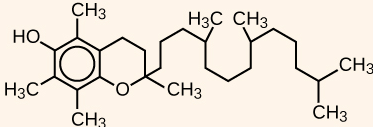
Consider statins for example—which is the name given to the class of drugs that reduces cholesterol levels. These compounds are essentially inhibitors of the enzyme HMG-CoA reductase. HMG-CoA reductase is the enzyme that synthesizes cholesterol from lipids in the body. By inhibiting this enzyme, the levels of cholesterol synthesized in the body can be reduced. Similarly, acetaminophen, popularly marketed under the brand name Tylenol, is an inhibitor of the enzyme cyclooxygenase. While it is effective in providing relief from fever and inflammation (pain), its mechanism of action is still not completely understood.

How are drugs developed? One of the first challenges in drug development is identifying the specific molecule that the drug is intended to target. In the case of statins, HMG-CoA reductase is the drug target. Drug targets are identified through painstaking research in the laboratory. Identifying the target alone is not sufficient; scientists also need to know how the target acts inside the cell and which reactions go awry in the case of disease.

Once the target and the pathway are identified, then the actual process of drug design begins. During this stage, chemists and biologists work together to design and synthesize molecules that can either block or activate a particular reaction. However, this is only the beginning: both if and when a drug prototype is successful in performing its function, then it must undergo many tests from in vitro experiments to clinical trials before it can get FDA approval to be on the market.

Many enzymes don't work optimally, or even at all, unless bound to other specific non-protein helper molecules, either temporarily through ionic or hydrogen bonds or permanently through stronger covalent bonds. Two types of helper molecules are **cofactors** and **coenzymes**. Binding to these molecules promotes optimal conformation and function for their respective enzymes. Cofactors are inorganic ions such as iron (Fe^{++}) and magnesium (Mg^{++}). One example of an enzyme that requires a metal ion as a cofactor is the enzyme that builds DNA molecules, DNA polymerase, which requires bound zinc ion (Zn^{++}) to function. Coenzymes are organic helper molecules, with a basic atomic structure made up of carbon and hydrogen,

which are required for enzyme action. The most common sources of coenzymes are dietary vitamins ([\[link\]](#)). Some vitamins are precursors to coenzymes and others act directly as coenzymes. Vitamin C is a coenzyme for multiple enzymes that take part in building the important connective tissue component, collagen. An important step in the breakdown of glucose to yield energy is catalysis by a multi-enzyme complex called pyruvate dehydrogenase. Pyruvate dehydrogenase is a complex of several enzymes that actually requires one cofactor (a magnesium ion) and five different organic coenzymes to catalyze its specific chemical reaction. Therefore, enzyme function is, in part, regulated by an abundance of various cofactors and coenzymes, which are supplied primarily by the diets of most organisms.

Dietary Vitamins	
Vitamin A 	Folic acid 
Vitamin B₁ 	Vitamin C 
Vitamin B₂ 	Vitamin D₂ (calciferol) 
Vitamin B₆ (pyridoxine) 	Vitamin E (alpha-tocopherol) 

Vitamins are important coenzymes or precursors of coenzymes, and are required for enzymes to function properly.

Multivitamin capsules usually contain mixtures of all the vitamins at different percentages.

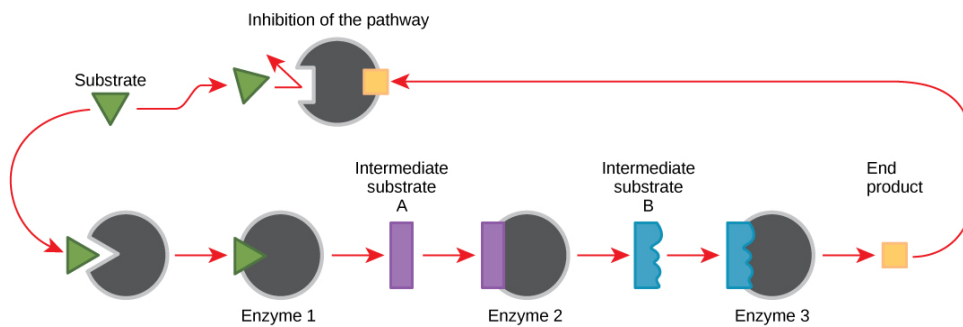
Enzyme Compartmentalization

In eukaryotic cells, molecules such as enzymes are usually compartmentalized into different organelles. This allows for yet another level of regulation of enzyme activity. Enzymes required only for certain cellular processes can be housed separately along with their substrates, allowing for more efficient chemical reactions. Examples of this sort of enzyme regulation based on location and proximity include the enzymes involved in the latter stages of cellular respiration, which take place exclusively in the mitochondria, and the enzymes involved in the digestion of cellular debris and foreign materials, located within lysosomes.

Feedback Inhibition in Metabolic Pathways

Molecules can regulate enzyme function in many ways. A major question remains, however: What are these molecules and where do they come from? Some are cofactors and coenzymes, ions, and organic molecules, as you've learned. What other molecules in the cell provide enzymatic regulation, such as allosteric modulation, and competitive and noncompetitive inhibition? The answer is that a wide variety of molecules can perform these roles. Some of these molecules include pharmaceutical and non-pharmaceutical drugs, toxins, and poisons from the environment. Perhaps the most relevant sources of enzyme regulatory molecules, with respect to cellular metabolism, are the products of the cellular metabolic reactions themselves. In a most efficient and elegant way, cells have evolved to use the products of their own reactions for feedback inhibition of enzyme activity. **Feedback inhibition** involves the use of a reaction product to regulate its own further production ([\[link\]](#)). The cell responds to

the abundance of specific products by slowing down production during anabolic or catabolic reactions. Such reaction products may inhibit the enzymes that catalyzed their production through the mechanisms described above.



Metabolic pathways are a series of reactions catalyzed by multiple enzymes. Feedback inhibition, where the end product of the pathway inhibits an upstream step, is an important regulatory mechanism in cells.

The production of both amino acids and nucleotides is controlled through feedback inhibition. Additionally, ATP is an allosteric regulator of some of the enzymes involved in the catabolic breakdown of sugar, the process that produces ATP. In this way, when ATP is abundant, the cell can prevent its further production. Remember that ATP is an unstable molecule that can spontaneously dissociate into ADP. If too much ATP were present in a cell, much of it would go to waste. On the other hand, ADP serves as a positive allosteric regulator (an allosteric activator) for some of the same enzymes that are inhibited by ATP. Thus, when relative levels of ADP are high compared to ATP, the cell is triggered to produce more ATP through the catabolism of sugar.

Additional Links

Khan Academy

The following links will take you to a series of videos on kinetics. The first link contains 4 videos on reaction rates and the second link contains 9 videos related to the relationship between reaction rates and concentration. These videos are supplemental and are provided to give you an outside resource to further explore enzyme kinetics.

- [Introduction to enzyme kinetics](#)
- [Reaction mechanism](#)

UCD Chemwiki

[Allosteric regulation](#)

Section Summary

Enzymes are chemical catalysts that accelerate chemical reactions at physiological temperatures by lowering their activation energy. Enzymes are usually proteins consisting of one or more polypeptide chains. Enzymes have an active site that provides a unique chemical environment, made up of certain amino acid R groups (residues). This unique environment is perfectly suited to convert particular chemical reactants for that enzyme, called substrates, into unstable intermediates called transition states. Enzymes and substrates are thought to bind with an induced fit, which means that enzymes undergo slight conformational adjustments upon substrate contact, leading to full, optimal binding. Enzymes bind to substrates and catalyze reactions in four different ways: bringing substrates together in an optimal orientation, compromising the bond structures of substrates so that bonds can be more easily broken, providing optimal environmental conditions for a reaction to occur, or participating directly in their chemical reaction by forming transient covalent bonds with the substrates.

Enzyme action must be regulated so that in a given cell at a given time, the desired reactions are being catalyzed and the undesired reactions are not. Enzymes are regulated by cellular conditions, such as temperature and pH. They are also regulated through their location within a cell, sometimes being compartmentalized so that they can only catalyze reactions under certain circumstances. Inhibition and activation of enzymes via other

molecules are other important ways that enzymes are regulated. Inhibitors can act competitively, noncompetitively, or allosterically; noncompetitive inhibitors are usually allosteric. Activators can also enhance the function of enzymes allosterically. The most common method by which cells regulate the enzymes in metabolic pathways is through feedback inhibition. During feedback inhibition, the products of a metabolic pathway serve as inhibitors (usually allosteric) of one or more of the enzymes (usually the first committed enzyme of the pathway) involved in the pathway that produces them.

Review Questions

Exercise:

Problem: Which of the following is not true about enzymes:

- a. They increase ΔG of reactions
- b. They are usually made of amino acids
- c. They lower the activation energy of chemical reactions
- d. Each one is specific to the particular substrate(s) to which it binds

Solution:

A

Exercise:

Problem: An allosteric inhibitor does which of the following?

- a. Binds to an enzyme away from the active site and changes the conformation of the active site, increasing its affinity for substrate binding
- b. Binds to the active site and blocks it from binding substrate
- c. Binds to an enzyme away from the active site and changes the conformation of the active site, decreasing its affinity for the substrate

d. Binds directly to the active site and mimics the substrate

Solution:

C

Exercise:

Problem:

Which of the following analogies best describe the induced-fit model of enzyme-substrate binding?

- a. A hug between two people
 - b. A key fitting into a lock
 - c. A square peg fitting through the square hole and a round peg fitting through the round hole of a children's toy
 - d. The fitting together of two jigsaw puzzle pieces.
-

Solution:

A

Free Response

Exercise:

Problem:

With regard to enzymes, why are vitamins necessary for good health? Give examples.

Solution:

Most vitamins and minerals act as coenzymes and cofactors for enzyme action. Many enzymes require the binding of certain cofactors or coenzymes to be able to catalyze their reactions. Since enzymes

catalyze many important reactions, it is critical to obtain sufficient vitamins and minerals from the diet and from supplements. Vitamin C (ascorbic acid) is a coenzyme necessary for the action of enzymes that build collagen, an important protein component of connective tissue throughout the body. Magnesium ion (Mg^{++}) is an important cofactor that is necessary for the enzyme pyruvate dehydrogenase to catalyze part of the pathway that breaks down sugar to produce energy. Vitamins cannot be produced in the human body and therefore must be obtained in the diet.

Exercise:**Problem:**

Explain in your own words how enzyme feedback inhibition benefits a cell.

Solution:

Feedback inhibition allows cells to control the amounts of metabolic products produced. If there is too much of a particular product relative to what the cell's needs, feedback inhibition effectively causes the cell to decrease production of that particular product. In general, this reduces the production of superfluous products and conserves energy, maximizing energy efficiency.

Glossary

active site

specific region of the enzyme to which the substrate binds

allosteric inhibition

inhibition by a binding event at a site different from the active site, which induces a conformational change and reduces the affinity of the enzyme for its substrate

coenzyme

small organic molecule, such as a vitamin or its derivative, which is required to enhance the activity of an enzyme

cofactor

inorganic ion, such as iron and magnesium ions, required for optimal regulation of enzyme activity

competitive inhibition

type of inhibition in which the inhibitor competes with the substrate molecule by binding to the active site of the enzyme

denature

process that changes the natural properties of a substance

feedback inhibition

effect of a product of a reaction sequence to decrease its further production by inhibiting the activity of the first enzyme in the pathway that produces it

induced fit

dynamic fit between the enzyme and its substrate, in which both components modify their structures to allow for ideal binding

substrate

molecule on which the enzyme acts

Bis2A 06.0 Energy in Living Systems v1.2

By the end of this section, you will be able to:

- Discuss the importance of electrons in the transfer of energy in living systems
- Explain how ATP is used by the cell as an energy source

Energy production within a cell involves many coordinated chemical pathways. Most of these pathways are combinations of oxidation and reduction reactions. Oxidation and reduction occur in tandem. An oxidation reaction strips an electron from an atom in a compound, and the addition of this electron to another compound is a reduction reaction. Because oxidation and reduction usually occur together, these pairs of reactions are called oxidation reduction reactions, or **redox reactions**.

Oxidation-Reduction Reactions

The chemical reactions underlying metabolism involve the transfer of electrons from one compound to another by processes catalyzed by enzymes. The electrons in these reactions commonly come from hydrogen atoms, which consist of an electron and a proton. A molecule gives up a hydrogen atom, in the form of a hydrogen ion (H^+) and an electron, breaking the molecule into smaller parts. The loss of an electron, or **oxidation**, releases a small amount of energy; both the electron and the energy are then passed to another molecule in the process of **reduction**, or the gaining of an electron. These two reactions always happen together in an **oxidation-reduction reaction** (also called a redox reaction)—when an electron is passed between molecules, the donor is oxidized and the recipient is reduced. Oxidation-reduction reactions often happen in a series, so that a molecule that is reduced is subsequently oxidized, passing on not only the electron it just received but also the energy it received. As the series of reactions progresses, energy accumulates that is used to combine P_i and ADP to form ATP, the high-energy molecule that the body uses for fuel.

Oxidation-reduction reactions are catalyzed by enzymes that trigger the removal of electrons (either one or two) from a substrate (sometimes the removal coincides with the removal of a proton) and transfers then to a second substrate, usually a coenzyme which can temporarily maintain the electrons (and sometimes protons) before transferring then to a second compound. There are two broad classes of coenzymes that work in redox reactions in the cell. The first are those coenzymes that can carry both electrons and protons, the two most common are **nicotinamide adenine dinucleotide (NAD^+)** and **flavin adenine dinucleotide (FAD)**. Their respective reduced coenzymes are **$NADH$** and **$FADH_2$** . A third coenzyme, **nicotinamide adenine dinucleotide phosphate ($NADP^+$)** is the primary reductant for **anabolic** reactions and has similar (yet distinct) properties to its unphosphorylated counterpart **NAD^+** . The second general group of enzymes (that contain co-factors such as heme) only carry electrons, and include **cytochromes**, and **Iron-Sulfur (Fe-S) proteins**.

Exercise:

Review Question

Problem:

Consider a red/ox reaction that requires NAD as a co-enzyme. As the reaction proceeds NAD^+ is reduced to $NADH$. What would happen to the reaction rate and the substrate concentration if the NAD^+ pool is fixed (a finite number of molecules in the cell)?

Solution:

As the reaction proceeds, NAD⁺ is reduced to NADH, if the NAD⁺ concentration is fixed, and NADH is not recycled the reaction will stop (or sit at some equilibrium) with no net increase in NADH because the NAD⁺ pool becomes so low.

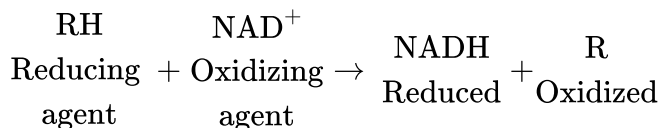
Electrons and Energy

The removal of an electron from a molecule, oxidizing it, results in a decrease in potential energy in the oxidized compound. The electron (sometimes as part of a hydrogen atom), does not remain unbonded, however, in the cytoplasm of a cell. Rather, the electron is shifted to a second compound, reducing the second compound. The shift of an electron from one compound to another removes some potential energy from the first compound (the oxidized compound) and increases the potential energy of the second compound (the reduced compound). The transfer of electrons between molecules is important because most of the energy stored in atoms and used to fuel cell functions is in the form of high-energy electrons. The transfer of energy in the form of electrons allows the cell to transfer and use energy in an incremental fashion—in small packages rather than in a single, destructive burst. This chapter focuses on the extraction of energy from food; you will see that as you track the path of the transfers, you are tracking the path of electrons moving through metabolic pathways.

Electron Carriers

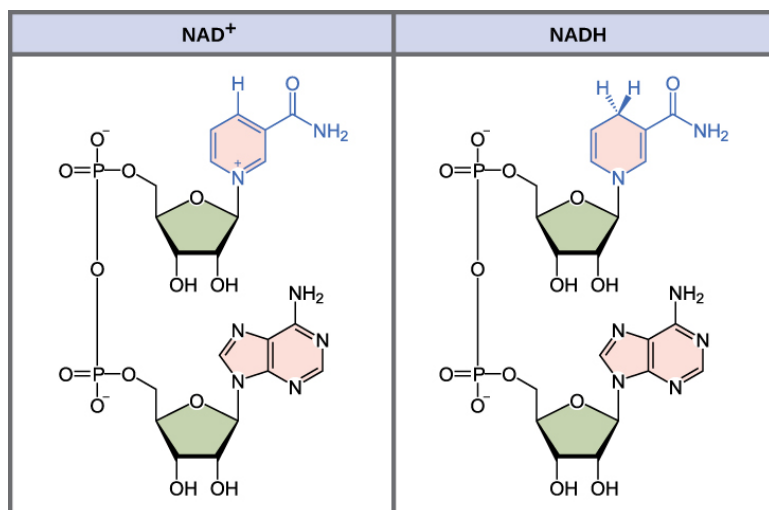
In living systems, a small class of compounds functions as electron shuttles: They bind and carry high-energy electrons between compounds in pathways. The principal electron carriers we will consider are derived from the B vitamin group and are derivatives of nucleotides. These compounds can be easily reduced (that is, they accept electrons) or oxidized (they lose electrons). Nicotinamide adenine dinucleotide (NAD⁺) ([\[link\]](#)) is derived from vitamin B3, niacin. NAD⁺ is the oxidized form of the molecule; NADH is the reduced form of the molecule after it has accepted two electrons and a proton (which together are the equivalent of a hydrogen atom with an extra electron).

NAD⁺ can accept electrons from an organic molecule according to the general equation:

Equation:

When electrons are added to a compound, they are reduced. A compound that reduces another is called a reducing agent. In the above equation, RH is a reducing agent, and NAD⁺ is reduced to NADH. When electrons are removed from compound, it is oxidized. A compound that oxidizes another is called an oxidizing agent. In the above equation, NAD⁺ is an oxidizing agent, and RH is oxidized to R.

Similarly, flavin adenine dinucleotide (FAD^+) is derived from vitamin B_2 , also called riboflavin. Its reduced form is FADH_2 . A second variation of NAD, NADP, contains an extra phosphate group. Both NAD^+ and FAD^+ are extensively used in energy extraction from sugars, and NADP plays an important role in anabolic reactions and photosynthesis.



The oxidized form of the electron carrier (NAD^+) is shown on the left and the reduced form (NADH) is shown on the right. The nitrogenous base in NADH has one more hydrogen ion and two more electrons than in NAD^+ .

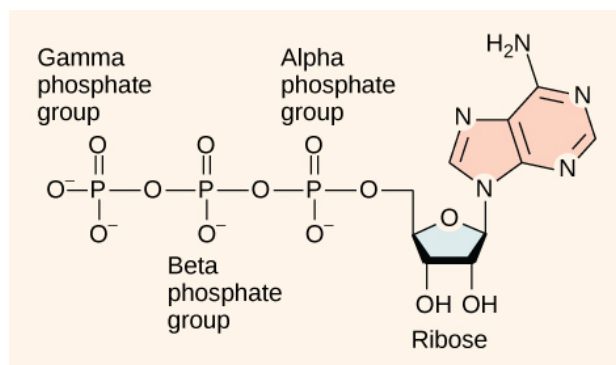
ATP in Living Systems

A living cell cannot store significant amounts of free energy. Excess free energy would result in an increase of heat in the cell, which would result in excessive thermal motion that could damage and then destroy the cell. Rather, a cell must be able to handle that energy in a way that enables the cell to store energy safely and release it for use only as needed. Living cells accomplish this by using the compound adenosine triphosphate (ATP). ATP is often called the “energy currency” of the cell, and, like currency, this versatile compound can be used to fill any energy need of the cell. How? It functions similarly to a rechargeable battery.

When ATP is broken down, usually by the removal of its terminal phosphate group, energy is released. The energy is used to do work by the cell, usually by the released phosphate binding to another molecule, activating it. For example, in the mechanical work of muscle contraction, ATP supplies the energy to move the contractile muscle proteins. Recall the active transport work of the sodium-potassium pump in cell membranes. ATP alters the structure of the integral protein that functions as the pump, changing its affinity for sodium and potassium. In this way, the cell performs work, pumping ions against their electrochemical gradients.

ATP Structure and Function

At the heart of ATP is a molecule of adenosine monophosphate (AMP), which is composed of an adenine molecule bonded to a ribose molecule and to a single phosphate group ([\[link\]](#)). Ribose is a five-carbon sugar found in RNA, and AMP is one of the nucleotides in RNA. The addition of a second phosphate group to this core molecule results in the formation of adenosine diphosphate (ADP); the addition of a third phosphate group forms adenosine triphosphate (ATP).



ATP (adenosine triphosphate) has three phosphate groups that can be removed by hydrolysis to form ADP (adenosine diphosphate) or AMP (adenosine monophosphate). The negative charges on the phosphate group naturally repel each other, requiring energy to bond them together and releasing energy when these bonds are broken.

The addition of a phosphate group to a molecule requires energy. Phosphate groups are negatively charged and thus repel one another when they are arranged in series, as they are in ADP and ATP. This repulsion makes the ADP and ATP molecules inherently unstable. The release of one or two phosphate groups from ATP, a process called **dephosphorylation**, releases energy.

Video on electron and electron/proton carriers

For a 7 minute YouTube video on the role of carriers in respiration click [here](#).

Energy from ATP

Hydrolysis is the process of breaking complex macromolecules apart. During hydrolysis, water is split, or lysed, and the resulting hydrogen atom (H⁺) and a hydroxyl group (OH⁻) are added to the larger molecule. The hydrolysis of ATP produces ADP, together with an inorganic phosphate ion (P_i), and the release of free energy. To carry out life processes, ATP is continuously broken down

into ADP, and like a rechargeable battery, ADP is continuously regenerated into ATP by the reattachment of a third phosphate group. Water, which was broken down into its hydrogen atom and hydroxyl group during ATP hydrolysis, is regenerated when a third phosphate is added to the ADP molecule, reforming ATP.

Obviously, energy must be infused into the system to regenerate ATP. Where does this energy come from? In nearly every living thing on earth, the energy comes from the metabolism of glucose. In this way, ATP is a direct link between the limited set of exergonic pathways of glucose catabolism and the multitude of endergonic pathways that power living cells.

Video Link

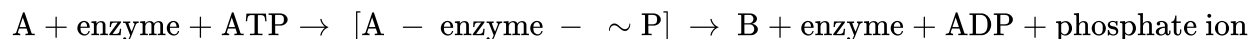
For a more detailed explanation of ATP and how this small molecule can store so much energy, take a look at this video (10 minutes) by clicking [here](#).

Phosphorylation

Recall that, in some chemical reactions, enzymes may bind to several substrates that react with each other on the enzyme, forming an intermediate complex. An intermediate complex is a temporary structure, and it allows one of the substrates (such as ATP) and reactants to more readily react with each other; in reactions involving ATP, ATP is one of the substrates and ADP is a product. During an endergonic chemical reaction, ATP forms an intermediate complex with the substrate and enzyme in the reaction. This intermediate complex allows the ATP to transfer its third phosphate group, with its energy, to the substrate, a process called phosphorylation.

Phosphorylation refers to the addition of the phosphate ($\sim P$). This is illustrated by the following generic reaction:

Equation:



When the intermediate complex breaks apart, the energy is used to modify the substrate and convert it into a product of the reaction. The ADP molecule and a free phosphate ion are released into the medium and are available for recycling through cell metabolism.

How do cells generate ATP

All cells require energy in the form of mobile packets. As we saw earlier in the class, these packets can be used to couple thermodynamically unfavorable reactions to drive the formation of specific products. Remember it costs energy to build, and the primary role of a cell is to make two cells. For what ever reason, almost 3.25 billion years of evolution has favored **ATP** as that mobile form of energy. It is the energy held within the **phosphoanhydride** bonds (the terminal or gamma and beta Phosphates) that store the energy. As shown in Figure 3, many common cellular compounds have such bonds and can also be used as an internal energy source with specific enzymes. Such compounds include all of the NTPs as well as common intermediates such as Phosphoenol pyruvate (PEP), which we will discuss later in glycolysis. Remember Not all carbon-Phosphate bonds are high energy, such as glucose-6-phosphate (figure 3).

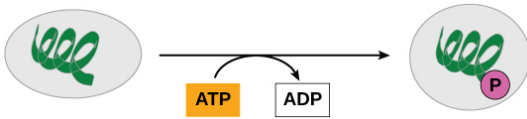
Compound	$\Delta G^{0'}$ kJ/mol
<hr/>	
> $\Delta G^{0'}$ kJ/mol	
Phosphoenol pyruvate	-51.6
1,3-bis-Phosphoglycerate	-52.0
Acetylphosphate	-44.8
ATP	-31.8
ADP	-31.8
Acetyl~CoA	-31
<hr/>	
< $\Delta G^{0'}$ kJ/mol	
AMP	-14.2
Glucose-6-P	-13.8

Table of common cellular phosphorylated molecules and their respective free energies

Because ATP is the primary source of mobile energy in the cell, a variety of mechanisms have emerged over the 3.25 billion years of evolution to form ATP. The majority of these mechanisms are modifications on two themes: direct synthesis of ATP or indirect synthesis of ATP. However all of the known reactions fall into two basic mechanisms: **Substrate Level Phosphorylation (SLP)** and **oxidative phosphorylation** and will be discussed in detail below and in the next few modules. Suffice it to say both mechanisms rely on the transfer of potential energy from one high energy compound (often called the energy source) to ADP, to synthesize ATP. This is either done directly, as in the case of Substrate level phosphorylation, or indirectly, as is the case for oxidative phosphorylation.

Substrate Level Phosphorylation

The simplest route to synthesize ATP is substrate level phosphorylation. ATP molecules are generated (that is, regenerated from ADP) as a direct result of a chemical reaction that occurs in catabolic pathways. A phosphate group is removed from an intermediate reactant in the pathway, and the free energy of the reaction is used to add the third phosphate to an available ADP molecule, producing ATP ([link](#)). This very direct method of phosphorylation is called **substrate-level phosphorylation**. It can be found in a variety of catabolic reactions, most notably in two specific reactions in glycolysis (which we will discuss specifically later). Suffice it to say what is required is a high energy intermediate whose oxidation is sufficient to drive the synthesis of ATP.



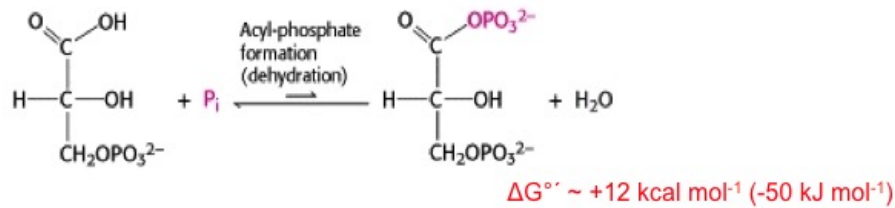
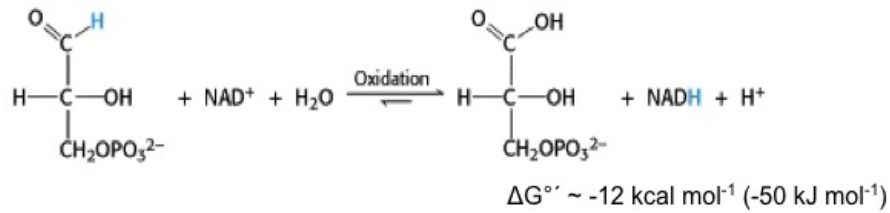
In phosphorylation reactions, the gamma phosphate of ATP is attached to a protein.

From an evolutionary perspective consider remember that the primordial ooze was hypothesized to be enriched with highly reduced small organic compounds. These reduced high energy compounds could have made an excellent initial energy source for early life. The simplest method of energy extraction being the oxidation of these compounds coupled to ATP synthesis; i.e. Substrate level phosphorylation. This simple method could theoretically have yielded large quantities of ATP for the cell along with smaller more oxidized organic compounds. Remember, we are currently only discussing ATP synthesis. If you consider this reaction, the coupling of the oxidation of reduced organic molecules to ATP synthesis, we are missing half the reaction, the compound to be reduced; ATP is not reduced during this reaction, it is simply forming a high energy bond. The electrons need to go somewhere, and the question where do they go?

The short answer is NAD^+ , those co-enzymes involved in red/ox reactions. Thus the first step in the synthesis of ATP is drive a Phosphate group onto the high energy compound by a red/ox reaction. The subsequent reduction of the energy source with the simultaneous phosphorylation produces two products, NADH (from the reduction of NAD^+) and the newly formed phosphorylated compound containing a high energy phosphate that can now be used to synthesize ATP in a second reaction. The best example of this in current metabolism is the reduction of glyceraldehyde-3-phosphate to 1,3-bisphosphoglycerate by NAD^+ . The formation of 1,3-bisphosphoglycerate and a high energy phosphoanhydride can then be used to phosphorylate ADP to ATP and production of 3-phosphoglycerate. This is diagrammed in figure 5 below.

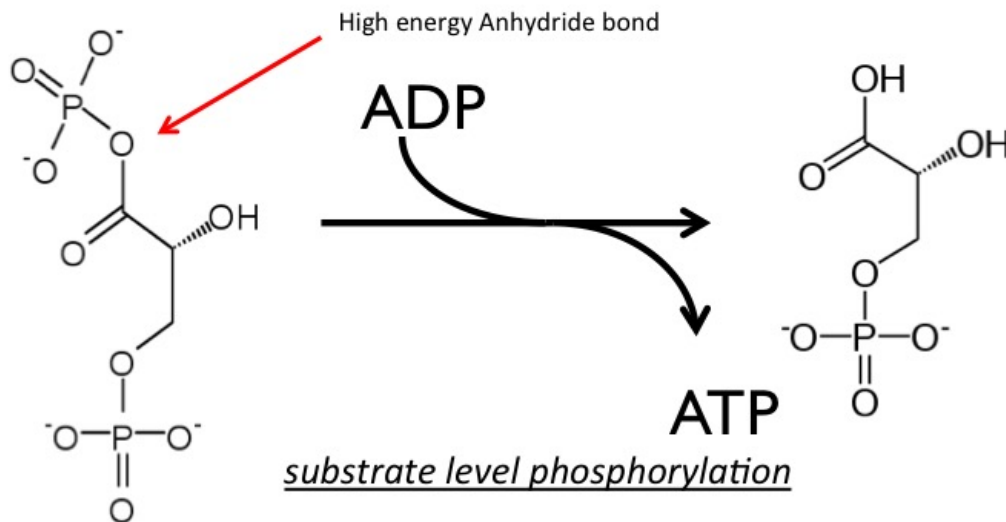
The oxidation of simultaneous phosphorylation of glyceraldehyde-3-phosphate:

This can be thought of as 2 reactions: Red/Ox and phosphorylation



The subsequent phosphate transfer reaction to ADP to form ATP in the reaction shown in figure 6 comes directly from the formation of 1,3-bisphosphoglycerate (described above). The arrow points out the high energy phosphoanhydride that is formed in the red/ox reaction. These two enzymatic reactions demonstrate how cells can transform one form of energy into a second, the potential energy from the substrates to potential energy in ATP. And of course the energy in ATP can then be used to help drive thermodynamically unfavorable reactions in the cell.

Direct phosphorylation of ADP



There is one last consideration you need to think about in our discussion of SLP. Consider the question posed earlier in exercise 1. Remember NAD⁺ is the original oxidizing agent used to form 1,3-bisphosphoglycerate from glyceraldehyde-3-phosphate. NAD⁺ is a co-enzyme and its levels are finite in the cell. So, as the reactions in figures 5 and 6 occur in the cell the levels of NAD⁺ fall and the levels of NADH rise. If left unchecked the cell has entered a death spiral. The answer is relatively simple, regenerate NAD⁺ by oxidizing NADH. This process is called **fermentation** and its role in metabolism is to reoxidize NADH to NAD⁺ forming a cycle between the two forms of the same molecule; as long as there is plenty of substrate to reduce NAD⁺ and enough substrate to oxidize NADH back to NAD⁺. We will discuss fermentation reactions in detail in a different module. But for this discussion, simply keep in mind that the cell must reoxidize NADH back to NAD⁺ in order to survive. Also keep in mind, that as with all aspects of energy metabolism, the basic process is very simple, NAD⁺ to NADH to NAD⁺ to....., yet a variety of rich complex reactions have evolved over time. This good news for us, because the end products of fermentation reactions include many foods and beverages we use every day. Think how boring life would be without bread, tea, beer and chocolate.

Oxidative Phosphorylation

In addition to substrate level phosphorylation, cells can generate ATP via an **electron transport chain** coupled to the proton dependent F₀F₁ ATPase. Such coupled systems require a **membrane** to both separate charge (electrical potential) and protons (chemical potential). This process is referred, called the **Chemiosmotic hypothesis** was proposed by [Peter Mitchell](#) in 1961.

While we will discuss this in detail later, in essence oxidative phosphorylation works by taking a reduced high energy compound, such as NADH+H⁺ or FADH₂, and transferring electrons in a

series of redox reactions to other compounds. The energy that is released is then "captured" by the translocation of protons (H^+) across the membrane. The net result is an "energized membrane" that separates charge, negative on the inside and positive on the outside (the electrical potential) and the separation of protons (chemical potential), protons concentration greater on the outside than inside of the membrane. The overall energized state of the membrane is then similar to a charged capacitor ready to do work. ATP generation occurs by the F₀F₁ membrane bound ATPase that translocates protons across the membrane discharging the chemical and electrical potentials with the simultaneous synthesis of ATP. For every three protons (H^+) translocated, the F₀F₁ATPase can synthesize 1 ATP.

Finally, oxidative phosphorylation does NOT require oxygen to function. The word oxidative in this case is in reference to redox reactions driving the process. We are very familiar with aerobic respiration which uses molecular oxygen as the terminal electron acceptor in some electron transport chains but this is a subset of reactions. As we will see later, other electron transport chains can use other compounds besides molecular oxygen as a terminal electron acceptor, such as nitrate or nitrite.

Photophosphorylation

Finally, many organisms can convert the energy from sun light to chemical energy (ATP) which is half of the reactions used in photosynthesis; the other half being the conversion of CO₂ to carbohydrates. In photosynthetic organisms, ATP and reducing power (production of NADPH+ H^+) is generated via a modified electron transport chain where the initial high energy electron(s) is derived from light energy instead of chemical energy from NADH+ H^+ .

While we will discuss this in detail later, in essence oxidative phosphorylation works by taking a reduced high energy compound, such as NADH or FADH₂, and transferring electrons in a series of red/ox reactions to other compounds. The energy that is released is then "captured" by the translocation of protons (H^+) across the membrane. The net result is an "energized membrane" that separates charge, negative on the inside and positive on the outside (the electrical potential) and the separation of protons (chemical potential), protons concentration greater on the outside than inside of the membrane. The overall energized state of the membrane is then similar to a charged capacitor ready to do work. ATP generation occurs by the F₀F₁ membrane bound ATPase that translocates protons across the membrane discharging the chemical and electrical potentials with the simultaneous synthesis of ATP. For every three protons (H^+) translocated, the F₀F₁ATPase can synthesize 1 ATP.

Section Summary

ATP functions as the energy currency for cells. It allows the cell to store energy briefly and transport it within the cell to support endergonic chemical reactions. The structure of ATP is that of an RNA nucleotide with three phosphates attached. As ATP is used for energy, a phosphate group or two are detached, and either ADP or AMP is produced. Energy derived from glucose catabolism is used to convert ADP into ATP. When ATP is used in a reaction, the third phosphate is temporarily attached to a substrate in a process called phosphorylation. The two processes of ATP regeneration that are used in conjunction with glucose catabolism are substrate-level phosphorylation and oxidative phosphorylation through the process of chemiosmosis.

Additional Links

Chemwiki Links

- [ATP](#)

Insert paragraph text here.

Review Questions

Exercise:

Problem: The energy currency used by cells is _____.

- a. ATP
- b. ADP
- c. AMP
- d. adenosine

Solution:

A

Exercise:

Problem: A reducing chemical reaction _____.

- a. reduces the compound to a simpler form
- b. adds an electron to the substrate
- c. removes a hydrogen atom from the substrate
- d. is a catabolic reaction

Solution:

B

Free Response

Exercise:

Problem:

Why is it beneficial for cells to use ATP rather than energy directly from the bonds of carbohydrates? What are the greatest drawbacks to harnessing energy directly from the bonds of several different compounds?

Solution:

ATP provides the cell with a way to handle energy in an efficient manner. The molecule can be charged, stored, and used as needed. Moreover, the energy from hydrolyzing ATP is delivered as a consistent amount. Harvesting energy from the bonds of several different compounds would result in energy deliveries of different quantities.

Glossary

chemiosmosis

process in which there is a production of adenosine triphosphate (ATP) in cellular metabolism by the involvement of a proton gradient across a membrane

dephosphorylation

removal of a phosphate group from a molecule

oxidative phosphorylation

production of ATP using the process of chemiosmosis and oxygen

phosphorylation

addition of a high-energy phosphate to a compound, usually a metabolic intermediate, a protein, or ADP

redox reaction

chemical reaction that consists of the coupling of an oxidation reaction and a reduction reaction

substrate-level phosphorylation

production of ATP from ADP using the excess energy from a chemical reaction and a phosphate group from a reactant

Bis2A 06.1 Red/Ox in metabolism v1.2

In this module we will review Red/Ox reactions and relate them to metabolic process. We will introduce the electron tower, a tool to be used to understand red/ox half reactions and the energy associated with different reactions.

Red/Ox reactions in biology

Earth's atmosphere contains about 20% molecular oxygen, O₂, a chemically reactive gas that plays an essential role in the metabolism of aerobic organisms and in many environmental processes that shape the world. The term **oxidation** was originally used to describe chemical reactions involving O₂, but its meaning has evolved to refer to a broad and important reaction class known as *oxidation-reduction (red/ox) reactions*. Our current working definition of **oxidation** is based on the ability of a compound to lose electrons, and removes all references to the involvement of molecular oxygen. A few examples of such reactions will be used to develop a clear picture of this classification of essential biochemical reactions.

The chemical reactions underlying metabolism involve the transfer of electrons from one compound to another by processes catalyzed by enzymes. The electrons in these reactions commonly come from hydrogen atoms, which consist of an electron and a proton. A molecule gives up a hydrogen atom, in the form of a hydrogen ion or proton, (H⁺) and an electron, breaking the molecule into smaller parts. During the loss of an electron(s), or **oxidation** from one compound, the electron(s) are then passed to another molecule in a process called **reduction**, or the gaining of an electron. These two reactions always happen together in an **oxidation-reduction reaction** (also called a red/ox reaction)—when electrons are passed between two molecules, the donor molecule is oxidized and the recipient molecule is reduced. These reactions are **exergonic**. Remember, an exergonic reaction is a chemical reaction where the change in the free energy is negative (there is a net release of free energy), indicating a spontaneous reaction. Oxidation-reduction reactions often happen in a series: A molecule that has just been reduced may be very quickly re-oxidized, passing on an electron to a new acceptor.

Remember the definitions of **oxidation** and **reduction**:

oxidation = loss of electrons

reduction = gain of electrons

Also remember, that if a compound is oxidized another compound must be reduced. The two process go together. The electrons have to go somewhere, we can not have free floating electrons in our system, they must be associated with a molecule or atom. This is an essential concept.

Red/Ox in metabolism

One of the primary sources of cellular energy comes from Oxidation-Reductions reactions, termed **red/ox**. During the movement of electrons from one molecule to a second, energy is released, and that energy can be used to work (translocate protons) or be stored (ATP synthesis) for future work. This is true as long as the electrons are passed from one compound to a second compound with a higher **reduction potential**, that is a compound that has a higher affinity for those electrons. The concept of reduction potential is explained below.

In metabolism, reduced compounds (organic or inorganic) can be used as electron donors, as long as the organism has the tools (enzymes) to use them. In other words whether a compound can be used as an electron source (or acceptor) is determined by whether that organism has the appropriate machinery, enzymes, to utilize the compound as a substrate. This is the basis of metabolic diversity. Some organisms to use all sorts of compounds as electron donors and electron acceptors. This allows them to live in environments others can not. While other organisms, such as us humans, are very limited as to what we can use: either NADH or FADH₂ for electron donors and only molecular oxygen (O₂ as a terminal electron acceptor.

In biological systems, oxidation-reduction reactions are catalyzed by enzymes that transfer electrons from the donor (the reduced compound or source of electrons) to the acceptor (the oxidized compound or electron acceptor). These enzymes can be single proteins to large, multiprotein complexes. Often times, the removal of electrons is simultaneously coupled

to the removal of a proton, or a hydrogen atom (one proton and one or two electrons). Many of these enzymes are called **dehydrogenases**, because they remove a hydrogen atom (a proton and one or two electrons)

The removed electrons and/or the associated proton are not "carried" on the protein per se but are carried on either a cofactor (sometimes referred to as a coenzyme) or a prosthetic group intimately coupled to the enzyme. The two most common coenzymes of oxidation-reduction reactions are **nicotinamide adenine dinucleotide (NAD)** and **flavin adenine dinucleotide (FAD)**. Their respective reduced coenzymes are **NADH** and **FADH₂**, which have a very low reduction potential and can be used to synthesize ATP or do aid in other forms of cellular work.

How are red/ox reactions used to generate usable energy for the cell

We have already discussed how some compounds can store a lot of energy while other compounds are relatively poor in energy stores. We know this intuitively, methane is explosive, methanol will catch on fire, and carbon dioxide is relatively inert. We also discussed that a distinguishing feature of "energy" rich compounds tend to more reduced than their "energy" poor relative. The difference between methane, methanol and carbon dioxide is the oxidation state of the carbon, -4 in methane, -2 in methanol and +4 in carbon dioxide. Methane is the most reduced state while carbon dioxide is the most oxidized state.

The same can be true for all sorts of compounds. In particular, for studying metabolism, we are interested in three types of molecules. The first are those compounds that can provided energy for the cell, such as glucose or methane, or even Fe^{2+} . These compounds are referred to as the **electron donor** and it is during their chemical modification by the cell that energy in the form of ATP can be generated.

The second type of molecules are those that cells can use as a final resting place for the electrons extracted from the electron source. These compounds are referred to as the **terminal electron acceptor**. These can be inorganic

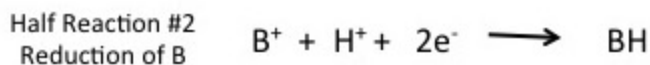
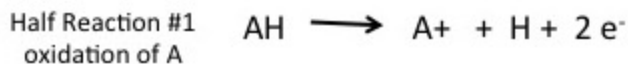
molecules or ions, such as molecular oxygen (O_2) or nitrate (NO_3^-). They can also be organic molecules such as lactate or acetate.

Finally, the third class of molecules are those that act as intermediaries and can act as both an electron acceptor or as an electron donor, depending upon the situation. Molecules such as $NAD^+/NADH$ or cytochrome_{ox}/cytochrome_{red} fall into this category. Think of members of this category as shuttle molecules, shuttling electrons from one compound to another.

How a cell utilizes these three types of molecules is how the cell generates its energy needs, whether it is through ATP generation or by the formation of an "energized membrane" or PMF as we will discuss later.

The Half Reaction

To understand how red/ox reactions work, we first need to discuss the concept of the half reaction. Two half reactions are required to make the full red/ox reaction. Each half reaction can be thought of as a description of what happens to one of the two molecules involved in the red/ox reaction. This is illustrated in figure 1 below. In this example compound AH is being oxidized by compound B^+ ; electrons are moving from AH to B^+ to generate A^+ BH. Each reaction can be thought of as two coupled half reactions: Where AH is being oxidized and a second reaction where B^+ is being reduced to BH.



Net result is the movement of electrons from A to B
B is more electronegative than A

Generic red/ox reaction where compound AH
is being oxidized by compound B^+

Exercise:

Problem: Use figure 1. In reaction #1, AH becomes:

- a. oxidized
- b. reduced

Solution:

a

Reduction Potential

Each half reaction represents a single species or compound to either lose or gain electrons (and a subsequent proton as shown in figure 1). In half reaction #1 AH loses a proton and 2 electrons: in the second half reaction, B^+ gains 2 electrons and a proton. In this example HA is oxidized to A^+ while B^+ is reduced to BH.

By convention we analyze and describe red/ox reactions with respect to reduction potentials that is, with respect to the ability of a compound to gain

electrons. Think of this in a similar way to how we think about Acid-Base reactions. By convention we use pH as a measure of the acidity or alkalinity. We view Acid-Base reactions through the lens of acidity. For red/ox reaction we view them through the lens of reduction potentials. That means for every reaction we ask, what is the intrinsic ability of that compound to “attract” or “pull” or “capture” electrons.

What is this intrinsic property to attract electrons? Remember **electronegativity**, the tendency of an atom or molecule to pull electrons. It is the basis of H-bonding and the ability of molecules to form dipoles or partial charges. This is the same quality or attribute we are discussing in red/ox reactions. Different compounds, based on their structure and composition have intrinsic and distinct attractions for electrons. This quality is termed **reduction potential** or E_0' and is a relative quantity. Relative in terms of comparison to a “**standard**” reaction. If a compound is more likely to take electrons from the standard, it has a higher or more positive reduction potential. The relative strength of the compound in comparison to the standard can be measured and is given in units of **Volts (V)** (sometimes written as electron volts or eV) or **milliVolts (mV)**. So the more positive the reduction potential the stronger the tendency is to take or attract electrons. The more negative the reduction potential the more likely the compound is to get rid of electrons.

So, lets look at the reactions in Figure 1 from a reduction potential perspective. In figure 2, we look at the same reaction and half reactions, but now we are looking at them through the lens of reduction potentials:

Reaction #1	$AH + B^+ \longrightarrow BH + A^+$	
Half Reaction #1 Oxidation of HA	$AH \longrightarrow A^+ + H + 2e^-$	
Half Reaction #2 Reduction of B ⁺	$B^+ + H^+ + 2e^- \longrightarrow BH$	
<hr/>		
		E'_0 in eV
Half Reaction #1 Reduction of A ⁺	$A^+ + H^+ + 2e^- \longrightarrow AH$	-0.32
Half Reaction #2 Reduction of B ⁺	$B^+ + H^+ + 2e^- \longrightarrow BH$	0.82

Generic Red/Ox reaction with half reactions written with reduction potential

Exercise:

E' values

Problem:

In the reaction written above (figure 2) the E' values are given for the two half reactions. Which of the following statements is accurate when comparing two half reactions?

- the half reaction with the more positive E' value will correspond with the electron acceptor
- the half reaction with the more negative E' value will correspond with the electron donor

- c. the half reaction with the greater reduction potential will correspond with the electron acceptor
- d. the half reaction with the greater reduction potential will correspond with the electron donor
- e. a and b
- f. a and c
- g. a, b and c
- h. a, b and d

Solution:

g

In figure 2 the top half of the figure shows the two half reactions as described in the original reaction. If we look at the substrates, HA and B^+ , in the reaction, HA is being oxidized to A^+ and B^+ is being reduced. If we rearrange the equations a bit, at least half reaction #1, such that we look at it from a reduction perspective we get the new half reaction shown in the bottom half of the figure. Now we are looking at the oxidized form of the molecule as the substrates and the reduced form as the products.

Once all reactions are written in the form for a reduction potential, it is easy to see who will take the electrons, the compound with the more positive reduction potential. In our generic case, it's B^+ . This nomenclature will be useful as we will see when we discuss and use the **electron tower** a tool to aid in understanding electron movements in biological systems.

How much energy can be used from a redox reaction: The energy story

While this is a "generic" or made up case, it serves as an example. When confronted with a potential red/ox problem, simply determine its energy story. First, decide which compounds are being oxidized and which are being reduced. Second, find the red/ox pairs, if a substrate is in the reduced form, find its oxidized cognate in the products. Third, rewrite the redox pairs such that the oxidized form of the cognates are all on the substrate side of the equation. And finally, determine the E_0' values for each half reaction.

The question now becomes how much potential energy the cell can derive from each red/ox reaction? The answer lies in the change of the reduction potentials of the two compounds. The change in the reduction potential for the reaction or E_0' for the reaction is the difference between the E_0' for the **oxidant** (the compound getting the electrons and causing the oxidation of the other compound) and the **reductant** (the compound losing the electrons and causing the reduction of the other compound). In our generic example in Figures 1 and 2 AH is the reductant and B^+ is the oxidant, remember electrons are flowing from HA to B^+ . Using the E_0' of -0.32 for the reductant and 0.82 for the oxidant the total change in E_0' or $\Delta E_0'$ is 1.14 eV. The change in reduction potential is readily convertible to changes in **Gibbs free energy**, ΔG , for the reaction as we will see below. In other words the change in reduction potential has a corresponding value in the change in free energy. While you do not need to know the details of how to convert from free energy to reduction potential and visa versa, suffice it to say, there is a correlation. In general a large positive $\Delta E_0'$ is proportional to a large negative ΔG . The reactions are exergonic and spontaneous.

What is the relationship between $\Delta E_0'$ and ΔG

Remember for a reaction to be exergonic the reaction needs to have a negative change in free energy or $-\Delta G$, this will correspond to a positive $\Delta E_0'$. In other words, when electrons flow "downhill" in a redox reaction from a compound with a higher (more positive) reduction potential to a second compound with a lower (less positive) reduction potential, they release free energy. The greater the difference between the redox potentials of two substances ($\Delta E_0'$), the greater the vigor with which electrons will flow spontaneously from the less positive to the more positive (more electronegative) substance. The greater the voltage, $\Delta E_0'$, between the two components, the greater the energy available when electron flow occurs. It is, in fact, possible to quantify the amount of free energy available. The relationship is:

Equation: $\Delta G = - n F (\text{kJ/V}) \Delta E (\text{V})$

where:

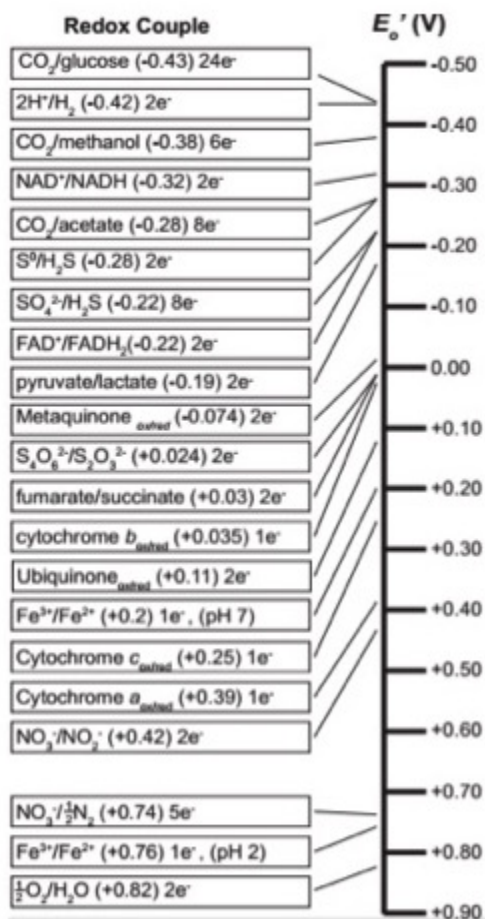
- n is the number of moles of electrons transferred
- F is the Faraday constant of 96.485 kJ/V. Sometimes it is given in units of kcal/V which is 23.062 kcal/V, which is the amount of energy (in kJ

or kcal) released when one mole of electrons passes through a potential drop of 1 volt

What you should notice is that ΔG and ΔE have different signage: When ΔG is positive, ΔE is negative and when ΔG is negative ΔE is positive. For a review see Red/Ox discussion in the Bis2A Discussion Manual.

The electron tower: A tool to be used for understanding red/ox

As you may have figured out, all kinds of compounds can be used in red/ox reactions in the cell. Making sense of all of this information and ranking potential red/ox pairs can be confusing. A tool has been developed to rate red/ox half reactions based on their E_0' values. Whether a particular compound can act as an electron donor (reductant) or electron acceptor (oxidant) still depend on what other compound it is interacting with. The electron tower ranks a variety of common compounds (their half reactions) from most negative E_0' , compounds that readily get rid of electrons, to the most positive E_0' , compound most likely to accept electrons. The tower organizes these half reactions based on the ability of electrons to accept electrons, with the most electronegative at the bottom of the tower. So the most negative E_0' values are at the top. In addition each half reaction is written by convention with the oxidized form on the left/ followed by the reduced form. For example the half reaction for the reduction of NAD^+ to NADH is written: $\text{NAD}^+/\text{NADH} + 2\text{e}^-$. An electron tower is shown in figure 2 below.



Common Red/ox tower used
in Bis2A

Video on electron tower

For a short video on how to use the electron tower in red/ox problems click [here](#). This video was made by Dr. Easlon for Bis2A students.

Exercise:

Reading a Redox tower

Problem:

The right and left sides of the chemical reactions in the redox tower are separated by a "/". The form of the compound on the left of the slash is _____, and the form of the compound on the right of the slash is _____.

- a. oxidized, reduced
- b. reduced, oxidized
- c. oxidized at the top of the tower, reduced at the bottom of the tower
- d. reduced at the top of the tower, oxidized at the bottom of the tower

Solution:

a

Remember, by convention the tower half reactions are written with the oxidized form of the compound on the left and the reduced form on the right. Compounds that make excellent electron donors, remember that first class of compounds we discussed earlier, are found at the top of the tower. Compounds such as Glucose and Hydrogen gas are excellent electron donors. Notice, that they are found on the right hand side of the red/ox pair half reactions. At the other end of the tower lies compounds that make excellent terminal electron acceptors, such as Oxygen and Nitrite, these compounds are found on the left side of the red/ox pair and have a positive E_0' value.

The tower is a tool to help determine whether a compound can act as an electron donor or an electron acceptor. Here lies the beauty of the that third class of compounds discussed above. These intermediate carriers, such as cytochromes or quinones, can act as either acceptor or donor depending upon their red/ox state and whether the other component in the red/ox reaction has a higher or lower E_0' value.

An example

Let's look at metaquinone_{ox/red}, it sits in the middle of the electron tower with an E_0' value of -0.074 eV. Metaquinone_{ox} can accept electrons from compounds that sit higher (above it) in the electron tower. In other words any reduced compound that has a lower E_0' value can donate electrons to metaquinone_{ox} to form metaquinone_{red} and the oxidized form of the original electron acceptor. Examples of compounds that could act as electron donors include FADH₂, an E_0' value of -0.22, or NADH, with an E_0' value of -0.32 eV. Remember the reduced forms are on the right hand side of the red/ox pair.

Once metaquinone has been reduced, it can now act as an electron donor to any compound that sits lower (below it) on the electron tower: any compound that has a higher E_0' value. Possible electron acceptors include cytochrome b_{ox} with an E_0' value of 0.035 eV; or ubiquinone_{ox} with an E_0' of 0.11 eV. Remember that the oxidized forms lie on the left side of the half reaction.

Exercise:

Exercise 1

Problem:

Which of the following could be used as an electron acceptor for Ubiquinone_{red}

- a. FAD
- b. NADH
- c. cytochrome a_{ox}
- d. cytochrome c_{red}

Solution:

C

Summary

Red/Ox reactions involve the movement of electrons from one compound to another. As electrons move from, the energy released can be captured by the cell to do work, such as synthesize ATP. Every red/ox reaction can be thought of as 2 half reactions, in one reaction a compound loses electrons and in the second reaction a different compound gains electrons. The amount of potential energy released is the difference in each half reactions reduction potential, E_0' . The electron tower is a tool that ranks different common half reactions (and therefore various compounds) based on how likely they are to donate or accept electrons. The lower, more negative, the electrochemical potential for each half reaction, the higher it sits in the electron tower. Reduced compounds can donate electrons to oxidized compounds that are below it on the electron tower. Oxidized compounds can accept electrons from any compound that are above it in the electron tower. The use of the electron tower will be more evident as we discuss electron transport chains in a few modules.

Bis2A 06.2 Oxidative Phosphorylation v1.2

By the end of this section, you will be able to:

- Describe how electrons move through the electron transport chain and what happens to their energy levels
- Explain how a proton (H^+) gradient is established and maintained by the electron transport chain

In the last module we discussed the various ways cells synthesize ATP and had a detailed discussion on substrate level phosphorylation. The second primary mechanism for ATP and energy formation is by oxidative phosphorylation. First and foremost, oxidative phosphorylation does not imply the use of oxygen, it can, but it does not have to use oxygen. It is called oxidative phosphorylation because it relies on red/ox reactions to generate a **membrane potential** that can then be used to do work. One of the "machines" that can be driven by the membrane potential, also referred to as the **proton motive force** or **PMF**, is the **F_1F_0 ATPase**. Unlike SLP, which directly synthesizes ATP, Oxidative Phosphorylation is an indirect mechanism. It is derived from a process that begins with moving electrons through a series of electron transporters or carriers that undergo red/ox reactions. The energy released from these reactions leads to the movement of protons across a membrane. This accumulation of protons on one side of the membrane "polarizes" or "charges" the membrane, with a net positive (protons) on one side of the membrane and a negative charge on the other side of the membrane. this is called an **electrical potential** due to the charge separation. In addition, the accumulation of protons also causes a pH gradient to form across the membrane and is referred to as the **chemical potential**. Together this is called an **electro-chemical gradient** across the membrane. Think of this as a cellular capacitor, as the charge and pH gradient grows more and more energy is stored and can be used to do work, such as driving the F_1F_0 ATPase and generating ATP indirectly.

Below the basic concepts of oxidative phosphorylation are described. Remember for ATP synthesis to occur two criteria must be met, the first is the formation of the membrane potential via a series of red/ox reactions, referred to as an **electron transport chain** and second, a membrane bound, proton driven F_1F_0 ATPase, that uses the potential energy from the PMF to

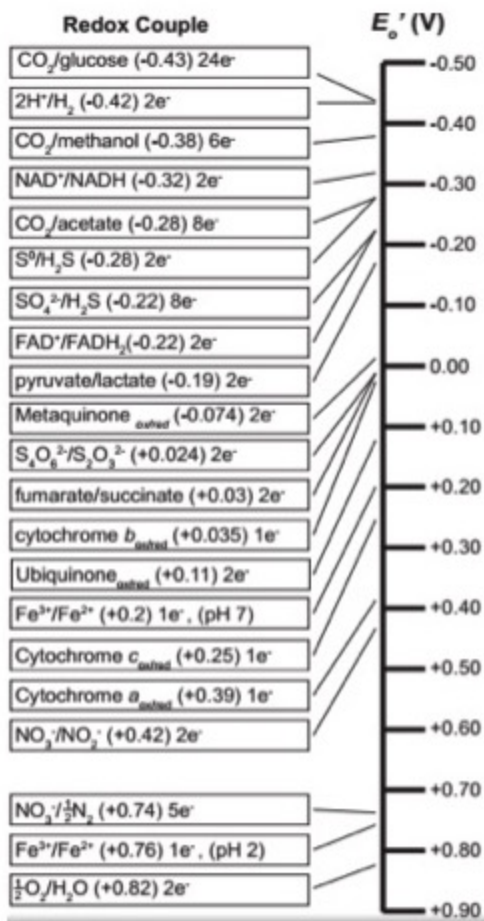
drive the formation of ATP by allowing protons to move from the higher concentration on one side of the membrane to the other side of lower concentration. Nowhere is molecular oxygen required for this to happen. Oxygen is a terrific terminal electron acceptor and allows for a very efficient way to generate a large PMF, however, other compounds such as hydrogen sulfide can also act as terminal electron acceptors. The eukaryotic mitochondrion has evolved an incredibly efficient electron transport chain to maximize ATP production for every 2 high energy electrons that enter the chain. While this mitochondrial electron transport chain is what we (eukaryotes) use, the diversity of the electron transport chain in nature is one of the most amazing features of life on this planet. Think about all of the unique and inhospitable places there are on this planet, yet some form of life can survive there. It makes one think about the possibility of life on other worlds. Remember all that is required is a donor of high energy electrons, carriers to move the electrons by red/ox reactions in a membrane, and a terminal electron acceptor. As we will discuss below, as long as the terminal electron acceptor has a higher affinity for the electrons than the electron donor, the electrons will move, and the energy can be captured by the cell.

Electron Transport Chain

Where do the electrons come from?

The **electron transport chain**, or **ETC**, is made up of a group of protein complexes that undergo a series of red/ox reactions to translocate protons across the membrane to generate a PMF. Electrons enter the ETS from a high energy electron donor, often times this is in the form of NADH or FADH₂, which are generated during catabolism (oxidation of carbon compounds, such as sugars or proteins or fats). Use the electron tower below (figure 1) as a reference guide to orient you as to where each component sits. Depending on the complexity of the ETC being used, electrons can enter at a variety of places depending upon the energy level of those entering electrons. To enter the ETC (electrons being donated to a red/ox complex within the chain), the electron donor must have a lower electronegativity than the electron acceptor (the complex that is taking the electrons). The donor will become oxidized and the acceptor will become reduced. The difference in the reduction potential between the donor and

acceptor is the measure of energy released. If sufficient energy is released the cell can use it to do work, and in the case of an ETC that work would include translocating a proton from one side of the membrane to the other, setting up a PMF.



Electron Tower

Note: electrons entering the ETC do not have to come from NADH or FADH₂. Many other compounds can serve as electron donors, the only requirement is that there exists an enzyme that can oxidize the electron donor and then reduce another compound. Even a small amount of energy can add up. For example there are bacteria that use H₂ as an electron donor.

This is not too difficult to believe because the half reaction $2\text{H}^+ + 2\text{e}^-/\text{H}_2$ has a reduction potential (E_0') of -0.42 eV. If these electrons are eventually donated to oxygen then the $\Delta E_0'$ of the reaction is 1.24 eV and that is equivalent to a lot of energy, a large negative ΔG ($-\Delta G$). Alternatively, there are some bacteria that can oxidize iron, Fe^{2+} at pH 7 to Fe^{3+} with a reduction potential (E_0') of +0.2 eV. These bacteria use oxygen as their terminal electron acceptor and in this case, the $\Delta E_0'$ of the reaction is approximately 0.62. Not so great, but still produces a $-\Delta G$. The bottom line is that depending on the electron donor and acceptor that the organism uses, a little or a lot of energy can be harvested and used by the cell per electrons donated to the electron transport chain.

What are the complexes of the ETC?

ETCs are made up of a series (at least one) of membrane associated (some are integral) red/ox complexes that move electrons from a donor source, such as NADH, to a final acceptor, such as oxygen (that's what we use). Each requires a reduced substrate as an electron donor and an oxidized substrate as the electron acceptor. In most cases the electron acceptor is a member of the enzyme complex. Once the complex is reduced, the complex can serve as the substrate (source of electrons) for the next reaction. In other words, think of the ETC as a series of complexes that passes electrons to the next complex, which eventually uses some oxidized compound as the final substrate (referred to as the **terminal electron acceptor**).

The total difference in the reduction potential of the electron donor and the final electron acceptor can be thought of as the total energy available for the system. How that energy is released, in one big chunk or in small aliquots is dependent upon the number of red/ox complexes the electrons will travel through. Each complex (in general) can be thought of as a release valve, where the energy being generated by the various red/ox reactions can be captured by the translocation of a proton. NOTE, not all complexes can generate enough energy to translocate a proton. The number of protons being translocated is important because in general it takes 3 protons to enter the F_1F_0 ATPase to generate 1 ATP molecule. The more protons translocated per 2 electrons that enter the chain, the more ATP that can be made.

How do ETC complexes transfer electrons?

As previously mentioned the ETC is composed of a series of complexes that undergo a series of red/ox reactions. These complexes are in fact multiprotein enzyme complexes referred to as **oxidoreductases** or simply **reductases**. The one exception to this is the terminal complex in aerobic respiration that uses molecular oxygen as the terminal electron acceptor. That enzyme complex is referred to as an **oxidase**. During the red/ox reaction the electrons are not carried directly on the proteins within the complex, but on a non-protein moiety called a **prosthetic group**. This is true for all of the electron carriers with the exception of quinones, which are a class of lipids that can directly be reduced or oxidized by the oxidoreductases. In this case, both the Quinone_{red} and the Quinone_{ox} is soluble within the membrane and can move from complex to complex. The prosthetic groups are directly involved in the red/ox reactions being catalyzed by their associated oxidoreductases. In general these prosthetic groups can be divided into two general types: those that carry both electrons and protons and those that only carry electrons.

The Electron and Proton carriers

- **Flavoproteins (Fp)**, these proteins contain an organic prosthetic group called a **flavin**, which is the actual moiety that undergoes the oxidation/reduction reaction. FADH₂ is an example of a Fp.
- **Quinones**, are a family of lipids which means they are soluble within the membrane.
- It should also be noted that NADH and NADPH are considered electron (2e⁻) and proton (2 H⁺) carriers.

Electron carriers

- **Cytochromes** are proteins that contain a heme prosthetic group. The Heme is capable of carrying a single electron.
- **Iron-Sulfur proteins** contain a non-heme iron-sulfur clusters that can carry an electron. The prosthetic group is often abbreviated as **Fe-S**

Aerobic versus Anaerobic respiration

In the world we live in, most of the organisms we interact with breath air, which is approximately 20% oxygen. Oxygen is our terminal electron acceptor. We call this process respiration, we breath in oxygen, our cells

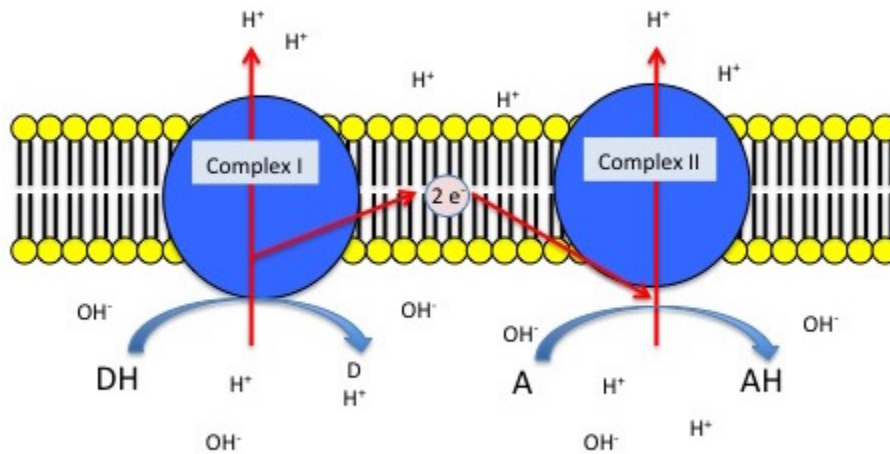
take it up and transport it into the mitochondria where it is used as the final acceptor of electrons from our electron transport chains. That is **aerobic respiration**: the process of using oxygen as a terminal electron acceptor in an electron transport chain.

However, many other organisms, all of them microbes (and include bacterial, archaeal and eukaryotic members) can use other compounds as terminal electron acceptors. These other compounds include common ions as nitrate (NO_3^-), reduction potential of +0.42, and nitrite (NO_2^-), reduction potential of +0.72, or tetrathionate ($\text{S}_4\text{O}_6^{2-}$) reduction potential of +0.024. When the terminal electron acceptor is **not** molecular oxygen (O_2) then the process is considered **anaerobic** and is referred to as **anaerobic respiration**. The ability of an organism to vary its terminal electron acceptor provides metabolic flexibility and can ensure better survival if any given terminal acceptor is in limited supply. Think about this, in the absence of oxygen we die; but an organism that can use a different terminal electron acceptor can survive.

A generic example of a simple, 2 complex ETC

Figure 1 shows a generic electron transport chain, composed of two integral membrane complexes; Complex I_{ox} and complex II_{ox}. A reduced high energy electron donor, designated HD (such as NADH or FADH_2) reduces complex I_{ox} giving rise to the oxidized form D (such as NAD or FAD). Simultaneously, a prosthetic group within complex I is now reduced (accepts the electrons) the energy released is used to translocate a proton from one side of the membrane to the other. The net result is that one surface becomes more negatively charged, due to an excess of hydroxyl ions (OH^-) and the other side becomes positively charged due to an increase in protons on the other side. Complex I_{red} can now reduce the prosthetic group in Complex II_{red} while simultaneously oxidizing Complex I_{red}. Electrons pass from Complex I to Complex II via red/ox reactions, regenerating Complex I_{ox} which can repeat the process. Complex II_{red} reduces A, the terminal electron acceptor to regenerate Complex II_{ox} and create the reduced form of the terminal electron acceptor. In this case, Complex II can also translocate a proton during the process. If A is molecular oxygen, water (H_2O) will be produced. This reaction would then be considered a model of an aerobic ETC. However, if A is nitrate, NO_3^-

then Nitrite, NO_2^- is produced (AH) and this would be an example of an anaerobic ETC.



Generic 2 complex electron transport chain. In the figure, DH is the electron donor (donor reduced) and D is the donor oxidized. A is the oxidized terminal electron acceptor and AH is the final product, the reduced form of the acceptor. As DH is oxidized to D, protons are translocated across the membrane, leaving an excess of hydroxyl ions (negatively charged) on one side of the membrane and protons (positively charged) on the other side of the membrane. The same reaction occurs in Complex II as the terminal electron acceptor is reduced to AH.

Exercise:
Thought question

Problem:

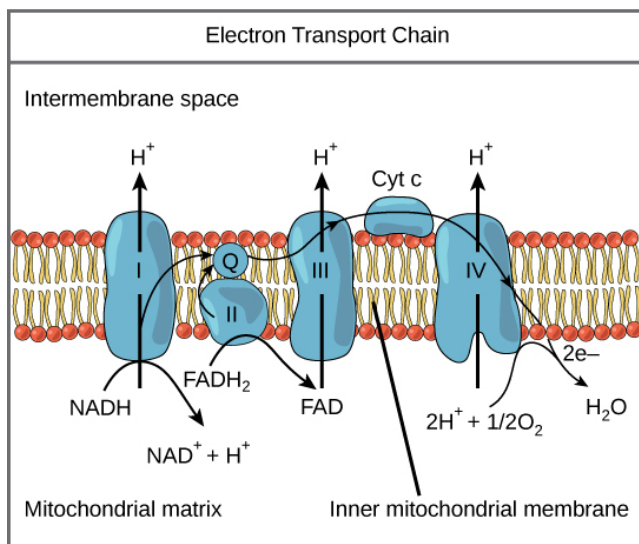
Based on Figure 2 above and using the electron tower in Figure 1, what is the difference in the electrical potential if (A) DH is NADH and A is O_2 and (B) DH is NADH and A is NO_3^- . Which pairs (A or B) provides the most amount of usable energy?

Solution:

To be discussed in class

Detailed look at aerobic respiration

The eukaryotic mitochondria has evolved a very efficient ETC. There are four complexes composed of proteins, labeled I through IV in [\[link\]](#), and the aggregation of these four complexes, together with associated mobile, accessory electron carriers, is called the electron transport chain. The electron transport chain is present in multiple copies in the inner mitochondrial membrane of eukaryotes and the plasma membrane of bacteria and arechaea.



The electron transport chain is a series of electron transporters

embedded in the inner mitochondrial membrane that shuttles electrons from NADH and FADH_2 to molecular oxygen. In the process, protons are pumped from the mitochondrial matrix to the intermembrane space, and oxygen is reduced to form water.

Complex I

To start, two electrons are carried to the first complex aboard NADH. This complex, labeled I, is composed of flavin mononucleotide (FMN) and an iron-sulfur (Fe-S)-containing protein. FMN, which is derived from vitamin B₂, also called riboflavin, is one of several prosthetic groups or co-factors in the electron transport chain. A **prosthetic group** is a non-protein molecule required for the activity of a protein. Prosthetic groups are organic or inorganic, non-peptide molecules bound to a protein that facilitate its function; prosthetic groups include co-enzymes, which are the prosthetic groups of enzymes. The enzyme in complex I is NADH dehydrogenase and is a very large protein, containing 45 amino acid chains. Complex I can pump four hydrogen ions across the membrane from the matrix into the intermembrane space, and it is in this way that the hydrogen ion gradient is established and maintained between the two compartments separated by the inner mitochondrial membrane.

Q and Complex II

Complex II directly receives FADH_2 , which does not pass through complex I. The compound connecting the first and second complexes to the third is **ubiquinone** (Q). The Q molecule is lipid soluble and freely moves through the hydrophobic core of the membrane. Once it is reduced, (QH_2),

ubiquinone delivers its electrons to the next complex in the electron transport chain. Q receives the electrons derived from NADH from complex I and the electrons derived from FADH_2 from complex II, including succinate dehydrogenase. This enzyme and FADH_2 form a small complex that delivers electrons directly to the electron transport chain, bypassing the first complex. Since these electrons bypass and thus do not energize the proton pump in the first complex, fewer ATP molecules are made from the FADH_2 electrons. The number of ATP molecules ultimately obtained is directly proportional to the number of protons pumped across the inner mitochondrial membrane.

Complex III

The third complex is composed of cytochrome b, another Fe-S protein, Rieske center (2Fe-2S center), and cytochrome c proteins; this complex is also called cytochrome oxidoreductase. Cytochrome proteins have a prosthetic group of heme. The heme molecule is similar to the heme in hemoglobin, but it carries electrons, not oxygen. As a result, the iron ion at its core is reduced and oxidized as it passes the electrons, fluctuating between different oxidation states: Fe^{++} (reduced) and Fe^{+++} (oxidized). The heme molecules in the cytochromes have slightly different characteristics due to the effects of the different proteins binding them, giving slightly different characteristics to each complex. Complex III pumps protons through the membrane and passes its electrons to cytochrome c for transport to the fourth complex of proteins and enzymes (cytochrome c is the acceptor of electrons from Q; however, whereas Q carries pairs of electrons, cytochrome c can accept only one at a time).

Complex IV

The fourth complex is composed of cytochrome proteins c, a, and a_3 . This complex contains two heme groups (one in each of the two cytochromes, a, and a_3) and three copper ions (a pair of Cu_A and one Cu_B in cytochrome a_3). The cytochromes hold an oxygen molecule very tightly between the iron

and copper ions until the oxygen is completely reduced. The reduced oxygen then picks up two hydrogen ions from the surrounding medium to make water (H_2O). The removal of the hydrogen ions from the system contributes to the ion gradient used in the process of chemiosmosis.

Links

Here are some useful links to videos on electron transport chains

- YouTube [Electron Transport Chain](#)
- YouTube [Electron Transport Chain #2](#)

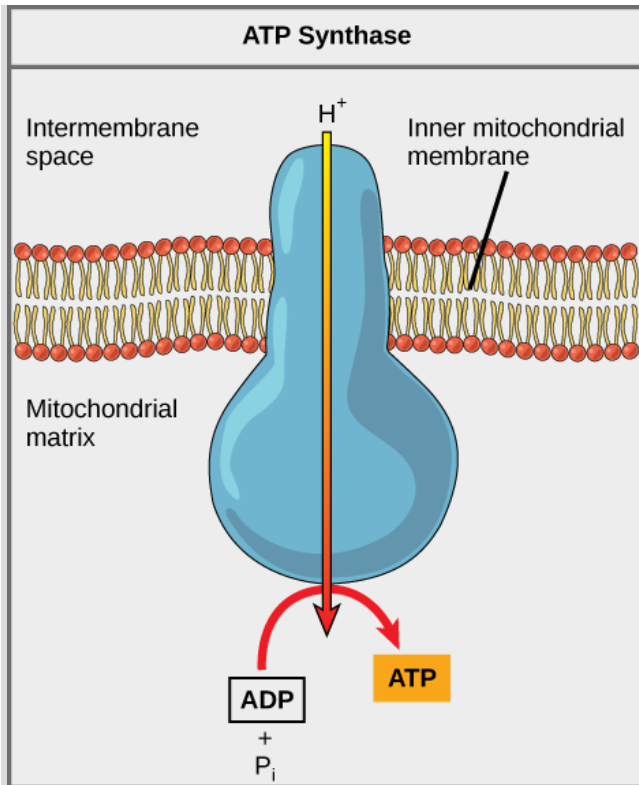
Chemiosmosis

In chemiosmosis, the free energy from the series of redox reactions just described is used to pump hydrogen ions (protons) across the membrane. The uneven distribution of H^+ ions across the membrane establishes both concentration and electrical gradients (thus, an electrochemical gradient), owing to the hydrogen ions' positive charge and their aggregation on one side of the membrane.

If the membrane were open to diffusion by the hydrogen ions, the ions would tend to diffuse back across into the matrix, driven by their electrochemical gradient. Recall that many ions cannot diffuse through the nonpolar regions of phospholipid membranes without the aid of ion channels. Similarly, hydrogen ions in the matrix space can only pass through the inner mitochondrial membrane through an integral membrane protein called ATP synthase ([\[link\]](#)). This complex protein acts as a tiny generator, turned by the force of the hydrogen ions diffusing through it, down their electrochemical gradient. The turning of parts of this molecular machine facilitates the addition of a phosphate to ADP, forming ATP, using the potential energy of the hydrogen ion gradient.

Note:

Art Connection



ATP synthase is a complex, molecular machine that uses a proton (H^+) gradient to form ATP from ADP and inorganic phosphate (P_i). (Credit: modification of work by Klaus Hoffmeier)

Dinitrophenol (DNP) is an uncoupler that makes the inner mitochondrial membrane leaky to protons. It was used until 1938 as a weight-loss drug. What effect would you expect DNP to have on the change in pH across the inner mitochondrial membrane? Why do you think this might be an effective weight-loss drug?

Chemiosmosis ([\[link\]](#)) is used to generate 90 percent of the ATP made during aerobic glucose catabolism; it is also the method used in the light

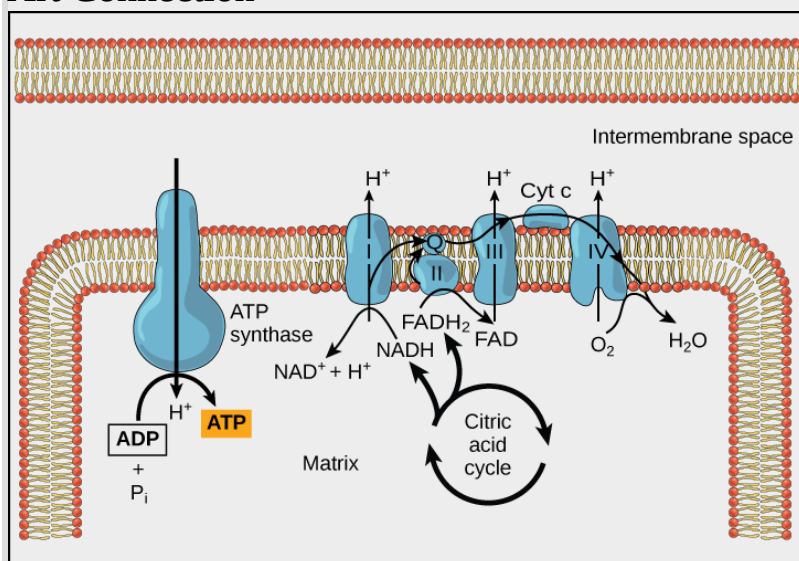
reactions of photosynthesis to harness the energy of sunlight in the process of photophosphorylation. Recall that the production of ATP using the process of chemiosmosis in mitochondria is called oxidative phosphorylation. The overall result of these reactions is the production of ATP from the energy of the electrons removed from hydrogen atoms. These atoms were originally part of a glucose molecule. At the end of the pathway, the electrons are used to reduce an oxygen molecule to oxygen ions. The extra electrons on the oxygen attract hydrogen ions (protons) from the surrounding medium, and water is formed.

Links

[How ATP is made from ATP synthase](#)

Note:

Art Connection



In oxidative phosphorylation, the pH gradient formed by the electron transport chain is used by ATP synthase to form ATP.

Cyanide inhibits cytochrome c oxidase, a component of the electron transport chain. If cyanide poisoning occurs, would you expect the pH of

the intermembrane space to increase or decrease? What effect would cyanide have on ATP synthesis?

ATP Yield

The number of ATP molecules generated from the catabolism of glucose varies. For example, the number of hydrogen ions that the electron transport chain complexes can pump through the membrane varies between species. Another source of variance stems from the shuttle of electrons across the membranes of the mitochondria. (The NADH generated from glycolysis cannot easily enter mitochondria.) Thus, electrons are picked up on the inside of mitochondria by either NAD^+ or FAD^+ . As you have learned earlier, these FAD^+ molecules can transport fewer ions; consequently, fewer ATP molecules are generated when FAD^+ acts as a carrier. NAD^+ is used as the electron transporter in the liver and FAD^+ acts in the brain.

Another factor that affects the yield of ATP molecules generated from glucose is the fact that intermediate compounds in these pathways are used for other purposes. Glucose catabolism connects with the pathways that build or break down all other biochemical compounds in cells, and the result is somewhat messier than the ideal situations described thus far. For example, sugars other than glucose are fed into the glycolytic pathway for energy extraction. Moreover, the five-carbon sugars that form nucleic acids are made from intermediates in glycolysis. Certain nonessential amino acids can be made from intermediates of both glycolysis and the citric acid cycle. Lipids, such as cholesterol and triglycerides, are also made from intermediates in these pathways, and both amino acids and triglycerides are broken down for energy through these pathways. Overall, in living systems, these pathways of glucose catabolism extract about 34 percent of the energy contained in glucose.

Section Summary

The electron transport chain is the portion of aerobic respiration that uses free oxygen as the final electron acceptor of the electrons removed from the

intermediate compounds in glucose catabolism. The electron transport chain is composed of four large, multiprotein complexes embedded in the inner mitochondrial membrane and two small diffusible electron carriers shuttling electrons between them. The electrons are passed through a series of redox reactions, with a small amount of free energy used at three points to transport hydrogen ions across a membrane. This process contributes to the gradient used in chemiosmosis. The electrons passing through the electron transport chain gradually lose energy. High-energy electrons donated to the chain by either NADH or FADH₂ complete the chain, as low-energy electrons reduce oxygen molecules and form water. The level of free energy of the electrons drops from about 60 kcal/mol in NADH or 45 kcal/mol in FADH₂ to about 0 kcal/mol in water. The end products of the electron transport chain are water and ATP. A number of intermediate compounds of the citric acid cycle can be diverted into the anabolism of other biochemical molecules, such as nonessential amino acids, sugars, and lipids. These same molecules can serve as energy sources for the glucose pathways.

Art Connections

Exercise:

Problem:

[\[link\]](#) Dinitrophenol (DNP) is an uncoupler that makes the inner mitochondrial membrane leaky to protons. It was used until 1938 as a weight-loss drug. What effect would you expect DNP to have on the change in pH across the inner mitochondrial membrane? Why do you think this might be an effective weight-loss drug?

Solution:

[\[link\]](#) After DNP poisoning, the electron transport chain can no longer form a proton gradient, and ATP synthase can no longer make ATP. DNP is an effective diet drug because it uncouples ATP synthesis; in other words, after taking it, a person obtains less energy out of the food he or she eats. Interestingly, one of the worst side effects of this drug is hyperthermia, or overheating of the body. Since ATP cannot be formed, the energy from electron transport is lost as heat.

Exercise:**Problem:**

[\[link\]](#) Cyanide inhibits cytochrome c oxidase, a component of the electron transport chain. If cyanide poisoning occurs, would you expect the pH of the intermembrane space to increase or decrease? What effect would cyanide have on ATP synthesis?

Solution:

[\[link\]](#) After cyanide poisoning, the electron transport chain can no longer pump electrons into the intermembrane space. The pH of the intermembrane space would increase, the pH gradient would decrease, and ATP synthesis would stop.

Review Questions**Exercise:**

Problem: What compound receives electrons from NADH?

- a. FMN
 - b. ubiquinone
 - c. cytochrome c_1
 - d. oxygen
-

Solution:

A

Exercise:

Problem: Chemiosmosis involves _____.

- a. the movement of electrons across the cell membrane

- b. the movement of hydrogen atoms across a mitochondrial membrane
 - c. the movement of hydrogen ions across a mitochondrial membrane
 - d. the movement of glucose through the cell membrane
-

Solution:

C

Free Response

Exercise:

Problem:

How do the roles of ubiquinone and cytochrome c differ from the other components of the electron transport chain?

Solution:

Q and cytochrome c are transport molecules. Their function does not result directly in ATP synthesis in that they are not pumps. Moreover, Q is the only component of the electron transport chain that is not a protein. Ubiquinone and cytochrome c are small, mobile, electron carriers, whereas the other components of the electron transport chain are large complexes anchored in the inner mitochondrial membrane.

Exercise:

Problem:

What accounts for the different number of ATP molecules that are formed through cellular respiration?

Solution:

Few tissues except muscle produce the maximum possible amount of ATP from nutrients. The intermediates are used to produce needed

amino acids, fatty acids, cholesterol, and sugars for nucleic acids. When NADH is transported from the cytoplasm to the mitochondria, an active transport mechanism is used, which decreases the amount of ATP that can be made. The electron transport chain differs in composition between species, so different organisms will make different amounts of ATP using their electron transport chains.

Glossary

ATP synthase

(also, F₁F₀ ATP synthase) membrane-embedded protein complex that adds a phosphate to ADP with energy from protons diffusing through it

prosthetic group

(also, prosthetic cofactor) molecule bound to a protein that facilitates the function of the protein

ubiquinone

soluble electron transporter in the electron transport chain that connects the first or second complex to the third

Bis2A 06.3 Photophosphorylation: The light reactions in photosynthesis
By the end of this section, you will be able to:

- Explain how plants absorb energy from sunlight
- Describe short and long wavelengths of light
- Describe how and where photosynthesis takes place within a plant

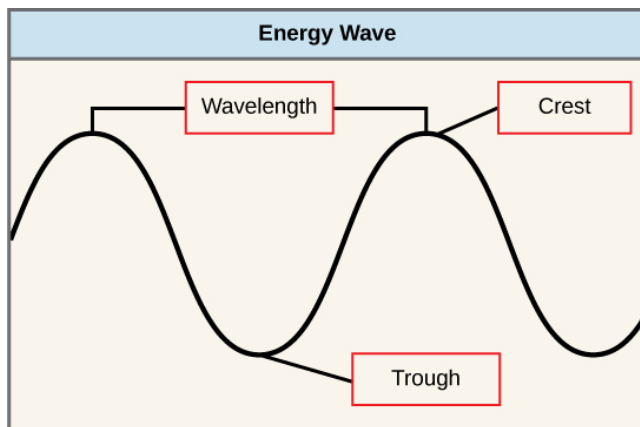
How can light be used to make food? When a person turns on a lamp, electrical energy becomes light energy. Like all other forms of kinetic energy, light can travel, change form, and be harnessed to do work. In the case of photosynthesis, light energy is converted into chemical energy, which photoautotrophs use to build carbohydrate molecules ([\[link\]](#)).



Photoautotrophs can capture light energy from the sun, converting it into the chemical energy used to build food molecules. (credit: Gerry Atwell)

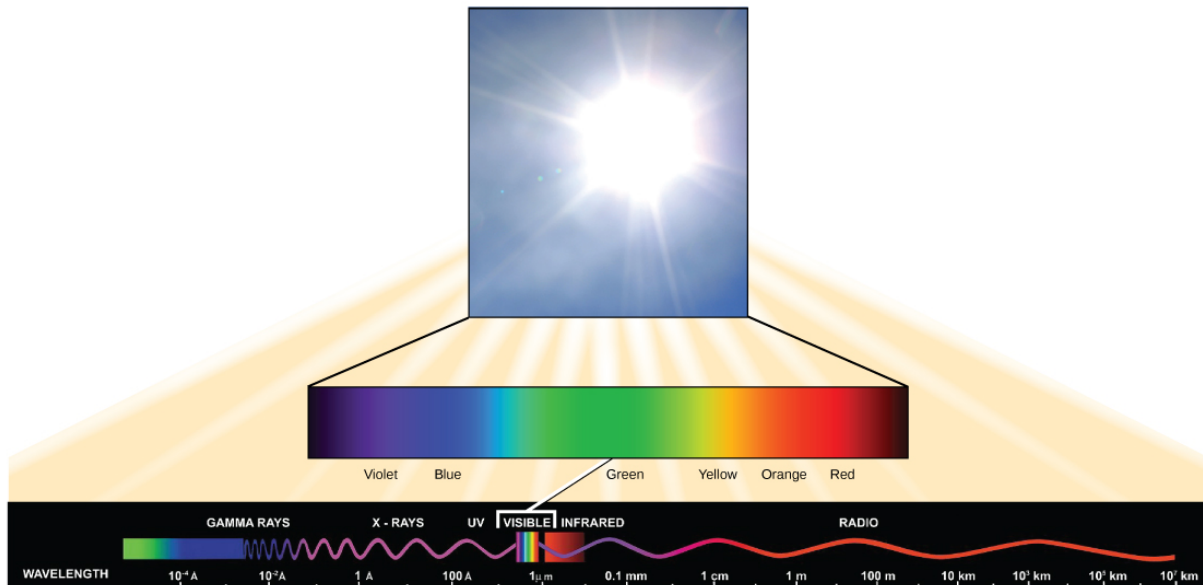
What Is Light Energy?

The sun emits an enormous amount of electromagnetic radiation (solar energy). Humans can see only a fraction of this energy, which portion is therefore referred to as “visible light.” The manner in which solar energy travels is described as waves. Scientists can determine the amount of energy of a wave by measuring its **wavelength**, the distance between consecutive points of a wave. A single wave is measured from two consecutive points, such as from crest to crest or from trough to trough ([\[link\]](#)).



The wavelength of a single wave is the distance between two consecutive points of similar position (two crests or two troughs) along the wave.

Visible light constitutes only one of many types of electromagnetic radiation emitted from the sun and other stars. Scientists differentiate the various types of radiant energy from the sun within the electromagnetic spectrum. The **electromagnetic spectrum** is the range of all possible frequencies of radiation ([\[link\]](#)). The difference between wavelengths relates to the amount of energy carried by them.



The sun emits energy in the form of electromagnetic radiation. This radiation exists at different wavelengths, each of which has its own characteristic energy. All electromagnetic radiation, including visible light, is characterized by its wavelength.

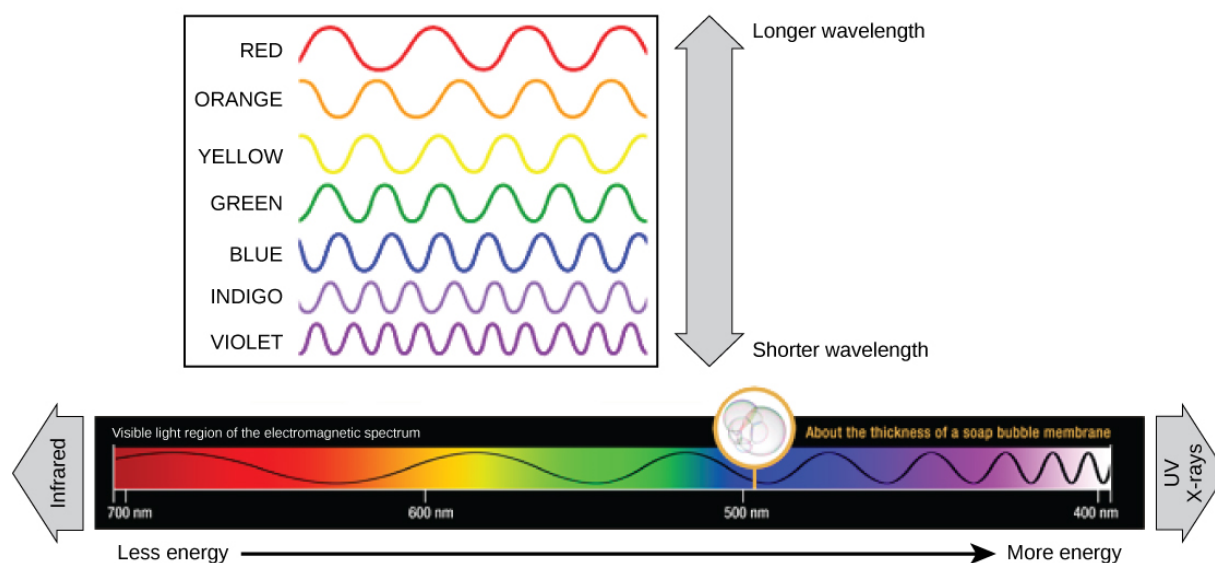
Each type of electromagnetic radiation travels at a particular wavelength. The longer the wavelength (or the more stretched out it appears in the diagram), the less energy is carried. Short, tight waves carry the most energy. This may seem illogical, but think of it in terms of a piece of moving a heavy rope. It takes little effort by a person to move a rope in long, wide waves. To make a rope move in short, tight waves, a person would need to apply significantly more energy.

The electromagnetic spectrum ([\[link\]](#)) shows several types of electromagnetic radiation originating from the sun, including X-rays and ultraviolet (UV) rays. The higher-energy waves can penetrate tissues and damage cells and DNA, explaining why both X-rays and UV rays can be harmful to living organisms.

Absorption of Light

Light energy initiates the process of photosynthesis when pigments absorb the light. Organic pigments, whether in the human retina or the chloroplast thylakoid, have a narrow range of energy levels that they can absorb. Energy levels lower than those represented by red light are insufficient to raise an orbital electron to a populatable, excited (quantum) state. Energy levels higher than those in blue light will physically tear the molecules apart, called bleaching. So retinal pigments can only “see” (absorb) 700 nm to 400 nm light, which is therefore called visible light. For the same reasons, plants pigment molecules absorb only light in the wavelength range of 700 nm to 400 nm; plant physiologists refer to this range for plants as photosynthetically active radiation.

The visible light seen by humans as white light actually exists in a rainbow of colors. Certain objects, such as a prism or a drop of water, disperse white light to reveal the colors to the human eye. The visible light portion of the electromagnetic spectrum shows the rainbow of colors, with violet and blue having shorter wavelengths, and therefore higher energy. At the other end of the spectrum toward red, the wavelengths are longer and have lower energy ([\[link\]](#)).



The colors of visible light do not carry the same amount of energy. Violet has the shortest wavelength and therefore carries the most

energy, whereas red has the longest wavelength and carries the least amount of energy. (credit: modification of work by NASA)

Understanding Pigments

Different kinds of pigments exist, and each has evolved to absorb only certain wavelengths (colors) of visible light. Pigments reflect or transmit the wavelengths they cannot absorb, making them appear in the corresponding color.

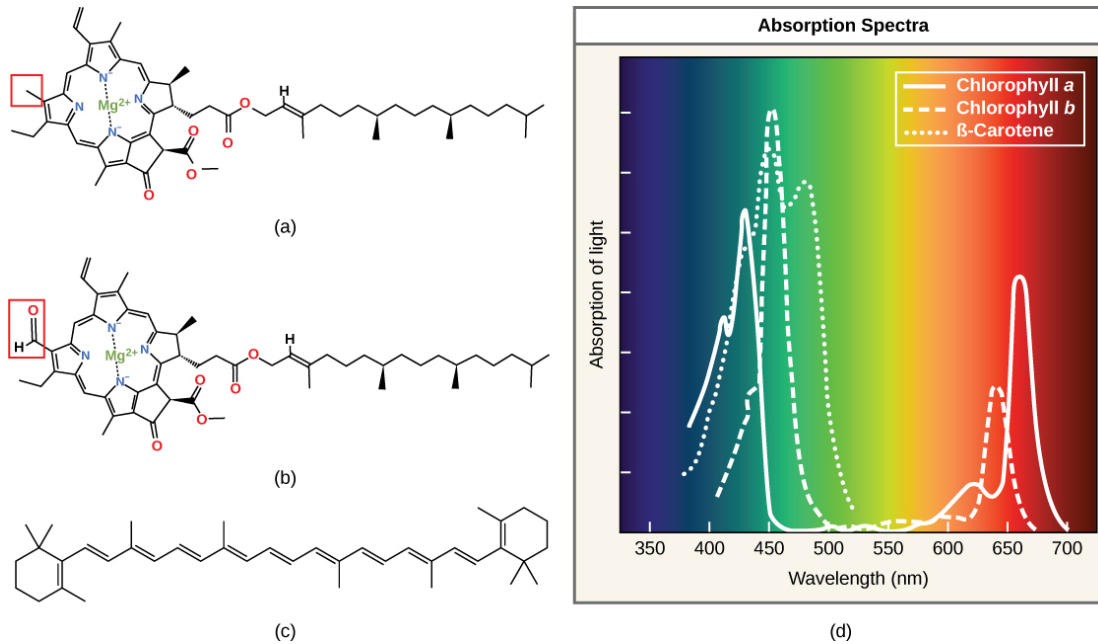
Chlorophylls and carotenoids are the two major classes of photosynthetic pigments found in plants and algae; each class has multiple types of pigment molecules. There are five major chlorophylls: *a*, *b*, *c* and *d* and a related molecule found in bacteria called **bacteriochlorophyll**.

Chlorophyll *a* and **chlorophyll *b*** are found in higher plant chloroplasts and will be the focus of the following discussion.

With dozens of different forms, carotenoids are a much larger group of pigments. The carotenoids found in fruit—such as the red of tomato (lycopene), the yellow of corn seeds (zeaxanthin), or the orange of an orange peel (β -carotene)—are used as advertisements to attract seed dispersers. In photosynthesis, **carotenoids** function as photosynthetic pigments that are very efficient molecules for the disposal of excess energy. When a leaf is exposed to full sun, the light-dependent reactions are required to process an enormous amount of energy; if that energy is not handled properly, it can do significant damage. Therefore, many carotenoids reside in the thylakoid membrane, absorb excess energy, and safely dissipate that energy as heat.

Each type of pigment can be identified by the specific pattern of wavelengths it absorbs from visible light, which is the **absorption spectrum**. The graph in [\[link\]](#) shows the absorption spectra for chlorophyll *a*, chlorophyll *b*, and a type of carotenoid pigment called β -carotene (which absorbs blue and green light). Notice how each pigment has a distinct set of

peaks and troughs, revealing a highly specific pattern of absorption. Chlorophyll *a* absorbs wavelengths from either end of the visible spectrum (blue and red), but not green. Because green is reflected or transmitted, chlorophyll appears green. Carotenoids absorb in the short-wavelength blue region, and reflect the longer yellow, red, and orange wavelengths.



(a) Chlorophyll *a*, (b) chlorophyll *b*, and (c) β -carotene are hydrophobic organic pigments found in the thylakoid membrane. Chlorophyll *a* and *b*, which are identical except for the part indicated in the red box, are responsible for the green color of leaves. β -carotene is responsible for the orange color in carrots. Each pigment has (d) a unique absorbance spectrum.

Many photosynthetic organisms have a mixture of pigments; using them, the organism can absorb energy from a wider range of wavelengths. Not all photosynthetic organisms have full access to sunlight. Some organisms grow underwater where light intensity and quality decrease and change with depth. Other organisms grow in competition for light. Plants on the rainforest floor must be able to absorb any bit of light that comes through,

because the taller trees absorb most of the sunlight and scatter the remaining solar radiation ([\[link\]](#)).

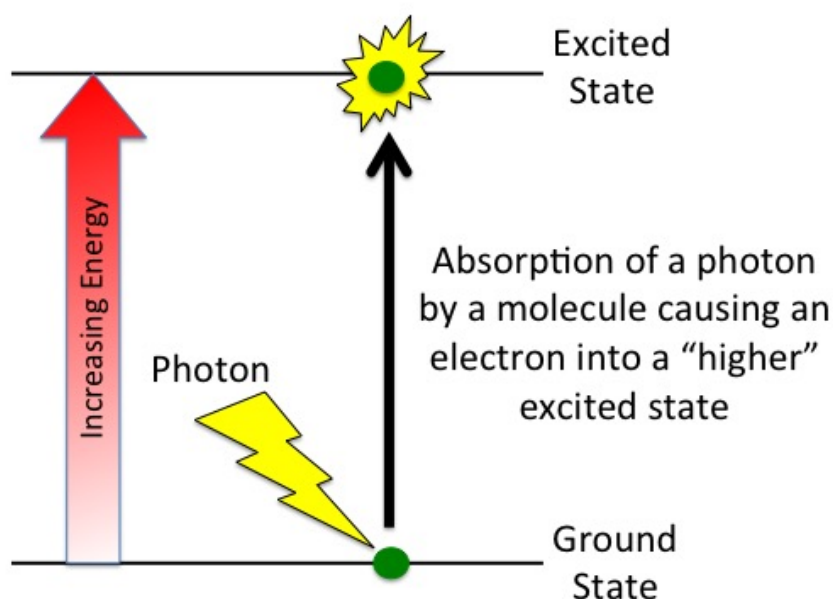


Plants that commonly grow in the shade have adapted to low levels of light by changing the relative concentrations of their chlorophyll pigments. (credit: Jason Hollinger)

When studying a photosynthetic organism, scientists can determine the types of pigments present by generating absorption spectra. An instrument called a **spectrophotometer** can differentiate which wavelengths of light a substance can absorb. Spectrophotometers measure transmitted light and compute from it the absorption. By extracting pigments from leaves and placing these samples into a spectrophotometer, scientists can identify which wavelengths of light an organism can absorb. Additional methods for the identification of plant pigments include various types of chromatography that separate the pigments by their relative affinities to solid and mobile phases.

What happens when a compound absorbs a photon of light?

When a compound absorbs a photon of light, the compound becomes "excited", in the sense that it has this extra energy. This is illustrated in figure 7 schematically. The compound has some ground state, it absorbs a photon and now contains this excess absorbed energy and is considered "excited". The question because what does the compound do with this excess absorbed energy and how does it get back to its "ground" state.

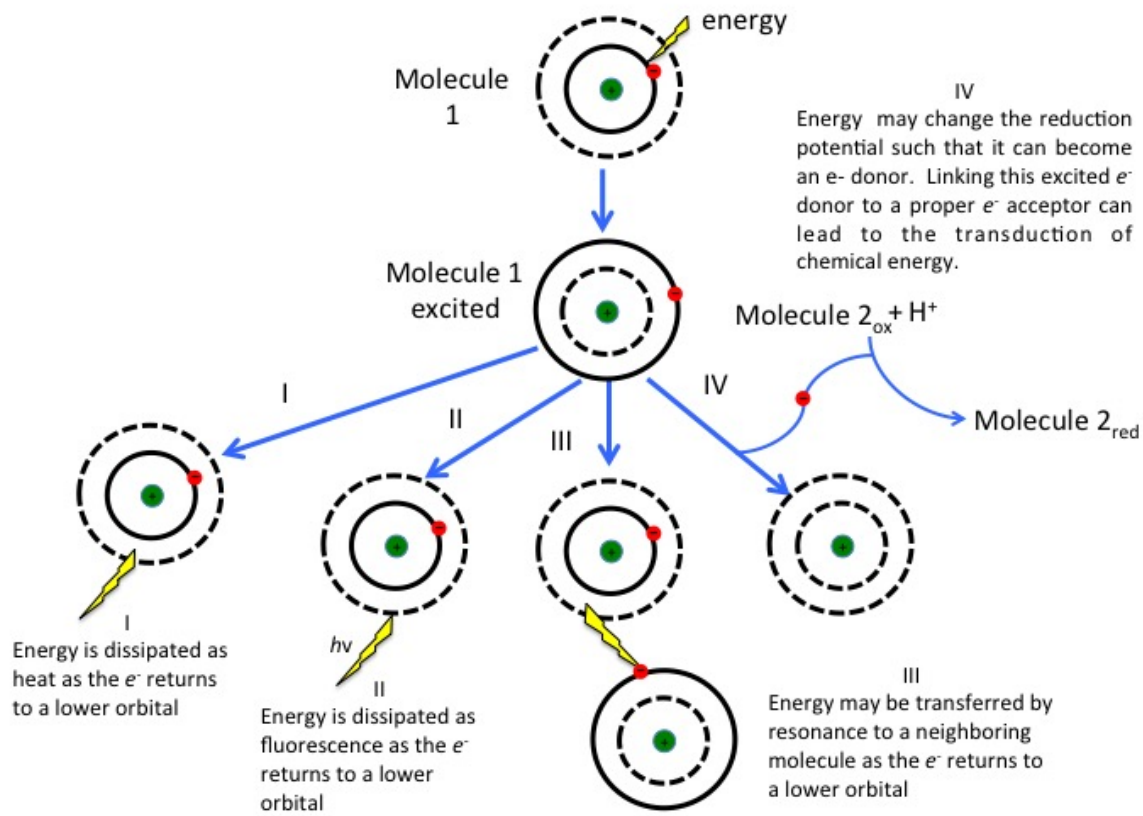


Energy diagram (energy story) of what happens to a molecule that absorbs a photon of light.

What does the excited atom or molecule do to return to its ground state. The energy in this molecule can then be dissipated in a variety of ways as the

excited electron decays back to its ground state. There are four possible outcomes, which are schematically diagrammed in Figure 8 below. These energy options are:

1. The energy can be dissipated as heat.
2. The energy can be dissipated as fluorescence as the e^- returns to a lower orbital.
3. The energy can be transferred by resonance to a neighboring molecule as the e^- returns to a lower orbital.
4. The energy can change the reduction potential such that it can become an e^- donor. Linking this excited e^- donor to a proper e^- acceptor can lead to the transduction of chemical energy this will be discussed in quite some detail in a later video and in lecture. For now let's just leave this as the ability of the excited molecule to be converted into chemical work. In other words the excited state can be used in red/ox reactions.



As the excited electron decays back to its original orbit, the energy can be released in a variety of ways. While many of the antenna or auxiliary pigments absorb light energy and transfer it to the reaction center (as depicted in option III in figure 8) it is what happens at the reaction center that we are most concerned with (option IV in figure 8). Here a chlorophyll or bacteriochlorophyll molecule absorbs the energy and an electron is excited. This energy transfer is sufficient to allow the reaction center to donate the electron in a red/ox reaction to a second molecule. This initiates the photophosphorylation electron transport reactions. The result is an oxidized reaction center that must now be reduced in order to start the process again. How this happens is the basis of electron flow in photophosphorylation and will be described in detail below.

Photophosphorylation a brief synopsis

Photophosphorylation is the process of converting light into chemical energy, ATP and NADPH. **Photosynthesis** is the integration of these light-reactions driving the reduction of CO₂ to sugars, specifically Glyceraldehyde-3-Phosphate, a triose. In this module we will focus on the first part of photosynthesis, the light-reactions or the generation of ATP and NADPH from light.

First and foremost it is important to realize that photophosphorylation and photosynthesis are very ancient sets of reactions. When we think of photosynthesis we mainly think of green plants; taking up CO₂ and giving off O₂. But this is a special, and from an evolutionary perspective, relatively new form of photophosphorylation. While extremely efficient and complicated, **oxygenic photophosphorylation**, the form of photophosphorylation that produces O₂ as a product, is only part of the picture of the evolution of photophosphorylation.

Photophosphorylation has its roots in the anaerobic world, between 3 billion and 1.5 billion years ago, when life was abundant in the absence of molecular oxygen. Photophosphorylation probably evolved relatively shortly after electron transport chains and **anaerobic respiration** began to provide metabolic diversity. Think of photophosphorylation this way: it is simply a form of an electron transport chain. The major difference is that instead of electrons being donated by a very strong reducing compound, such as NADH, light energy is used to "energize" an electron into a "high energy state". This "energized" electron can be donated to an electron transport chain, and as it decays, that is, as it passes from one electron carrier to another via red/ox reactions protons are pumped across a membrane. The pumping of these protons across a membrane leads to the generation of a PMF, which in turn results in the production of ATP. If enough light energy or **photons** can be absorbed and transferred to electrons, and if those electrons can have a lower (that is a more negative) reduction potential than NADP/NADPH, then they can be used reduce NADP to form NADPH. Therefore, photophosphorylation requires a compound that can absorb light energy or photons, use that energy to excite an electron and then donate that excited electron to NADPH. That compound is chlorophyll or bacteriochlorophyll. The final piece of the photophosphorylation story is finding something to reduce the oxidized

bacteriochlorophyll, under anaerobic conditions, reduced sulfur compounds such as SH_2 and even elemental S^0 are excellent electron donors (look at the redox tower provided in figure 9 to see more potential electron donors).

These early, simple **anoxygenic photophosphorylation** pathways could either make NADPH, in a process called **noncyclic** photophosphorylation or ATP, in a processes called **cyclic photophosphorylation** per donated electron. At some point, about 1.5 billion years ago, a chlorophyll molecule evolved that when oxidized (when a photon of light was absorbed and transferred to the electron which is ejected) had a higher (more positive) reduction potential than O_2 . Which meant that the oxidized form of chlorophyll could be reduced by water and generate molecular oxygen. That event changed the shape of the planet for ever. That event, the great **oxygen event** now begins to accumulate molecular oxygen, a toxic, highly corrosive and reactive compound, into the environment and life on this planet would change forever.

Simple Anoxygenic Photophosphorylation Systems

Introduction

For the early photophosphorylation systems no oxygen was generated. These reactions evolved in anaerobic environments, there was very little molecular oxygen available. Two sets of reactions evolved under these conditions, both directly from anaerobic respiratory chains. These are known as the **light reactions** because they require the activation of an electron (an excited electron) from the absorption of light energy by bacteriochlorophyll. The light reactions are categorized either as **cyclic** or as **noncyclic** photophosphorylation. To help you better understand the similarities of photophosphorylation to respiration, figure 9 below is an electron tower that will be useful in our discussion of photosynthesis.

Electron Tower

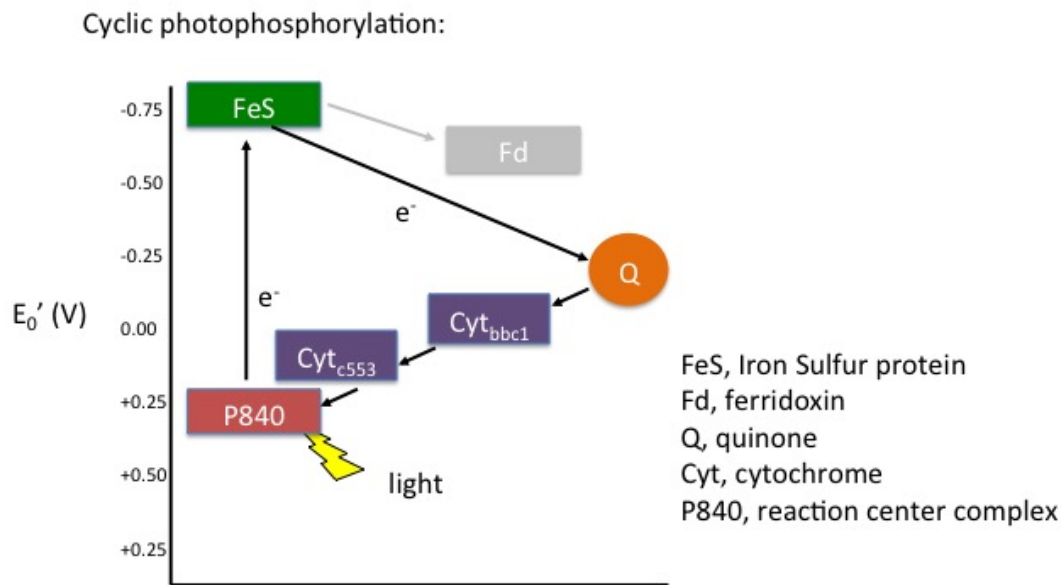
OXIDIZED	REDUCED	E'
PSI-excited	PSI-excited	-1.20
Ferredoxin (ox)	Ferredoxin (red)	-0.70
acetate	acetaldehyde	-0.60
CO ₂	Glucose	-0.43
FNR (ox)	FNR (red)	-0.43
2H	H ₂	-0.42
NADP ⁺ + 2H	NADPH + H	-0.32
PSII-excited	PSII-excited	-0.30
Plastoquinone	Plastoquinone	-0.14
Fumarate + 2H	Succinate	+0.03
Ubiquinone (ox)	Ubiquinone (red)	+0.10
CytochromeC	CytochromeC	+0.25
CytochromeB (ox)	CytochromeB (red)	+0.25
CytochromeF	CytochromeF	+0.37
PSI-not excited	PSI-not excited	+0.37
Nitrate	Nitrite	+0.43
1/2O ₂ + 2H	H ₂ O	+0.82
PSII-not excited	PSII-not excited	+1.1

Electron tower that has a variety of common photophosphorylation components. PSI and PSII refer to Photosystems I and II of the oxygenic photophosphorylation pathways. For the examples in Figure 8 and Figure 9 P840 is similar in reduction potential as is PSI.

Cyclic Photophosphorylation

In cyclic photophosphorylation the bacteriochlorophyll_{red} molecule absorbs enough light energy to energize and eject an electron forming bacteriochlorophyll_{ox}. The electron reduces a carrier molecule in the reaction center which in turn reduces a series of carriers via red/ox reactions. These carriers are the same carriers found in respiration. If the change in reduction potential from the various red/ox reactions are sufficiently large, protons, H⁺ are translocated across the membrane. Eventually the electron is used to reduce bacteriochlorophyll_{ox} and the

whole process can start again. This is called cyclic photophosphorylation because the electrons make a complete circuit: bacteriochlorophyll is the source of electrons and is the final electron acceptor. ATP is produced via the **F₁F₀ ATPase**. The schematic in figure 10 below demonstrates how cyclic photophosphorylation works.



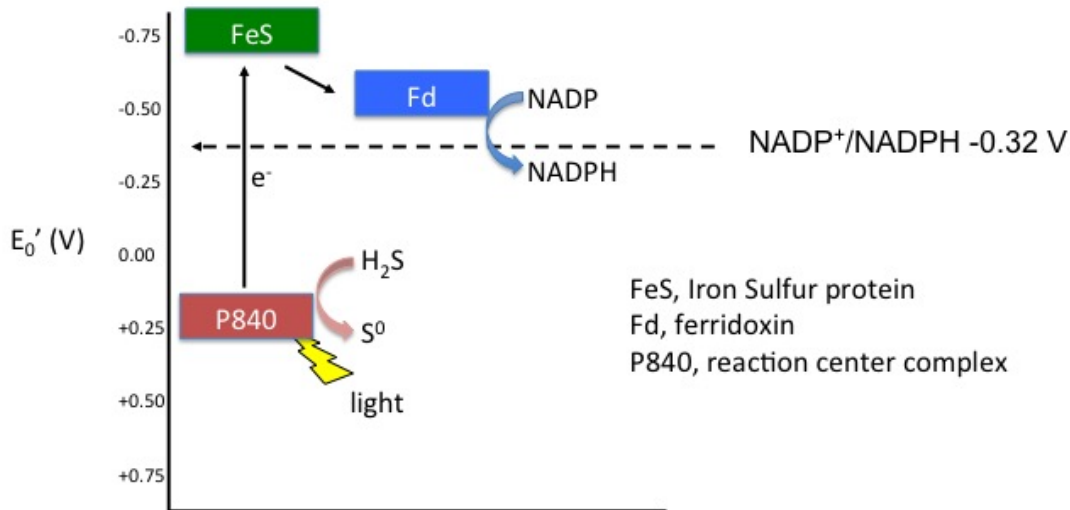
Cyclic Photophosphorylation. The reaction center P840 absorbs light energy and becomes excited, denoted with an *. The excited electron is ejected and used to reduce an FeS protein leaving an oxidized reaction center. The electron is transferred to a quinone, then to a series of cytochromes which in turn reduces the P840 reaction center. The process is cyclical. Note the gray arrow coming from the FeS protein going to a ferridoxin (Fd), also in gray. This represents an alternative pathway the electron can take and will be discussed below in non-

cyclic photophosphorylation. **NOTE** the same electron that leaves the P480 reaction center is not necessarily the same electron that eventually finds its way back to reduce the oxidized P840.

Non-cyclic photophosphorylation

In cyclic photophosphorylation electrons cycle from bacteriochlorophyll (or chlorophyll) to a series of electron carriers and eventually back to bacteriochlorophyll (or chlorophyll): there is no loss of electrons, they stay in the system. In non-cyclic photophosphorylation the electrons are removed from the system, they eventually end up on NADPH. That means there needs to be a source of electrons, a source that has a higher reduction potential than bacteriochlorophyll (or chlorophyll) that can donate electrons to bacteriochlorophyll_{ox} to reduce it. An electron tower is provided below so you can see what compounds can be used to reduce the oxidized form of bacteriochlorophyll. The second requirement, is that when bacteriochlorophyll becomes oxidized and the electron is ejected it must reduce a carrier that has a lower (more negative) reduction potential than NADP/NADPH (see the electron tower). In this case, electrons can flow from energized bacteriochlorophyll to NADP forming NADPH and oxidized bacteriochlorophyll. Electrons are lost from the system and end up on NADPH, to complete the circuit bacteriochlorophyll_{ox} is reduced by an external electron donor, such as H₂S or elemental S⁰. This is diagrammed in figure 11 below.

Non-cyclic photophosphorylation:



Non-cyclic photophosphorylation. In this example, the P840 reaction center absorbs light energy and becomes energized, the emitted electron reduced a FeS protein and in turn reduces ferridoxin. Reduced ferridoxin (Fd_{red}) can now reduce NADP to form NADPH. The electrons are now removed from the system, finding their way to NADPH. The electrons need to be replaced on P840, which requires an external electron donor. In this case, H_2S serves as the electron donor.

Thought questions.

It should be noted that per electron donated to the system, either NADPH or ATP is made, but not both. This puts a limit on the versatility of the system. But what would happen if both systems coexisted simultaneously? That is, if both ATP and NADPH could be formed from one electron? Additionally,

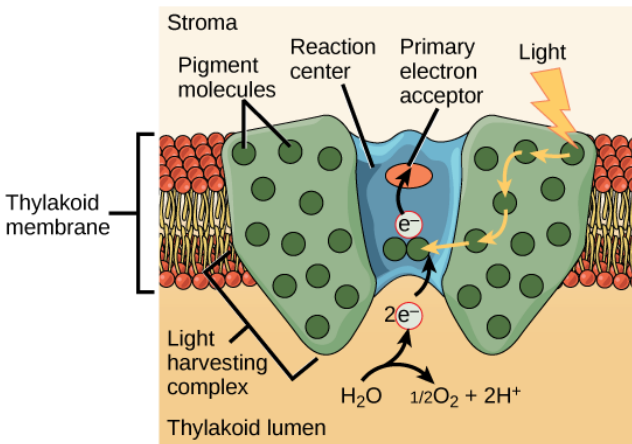
these systems require compounds such as reduced sulfur to act as electron donors, not necessarily widely found compounds. What would happen if a chlorophyll_{ox} molecule would have a reduction potential higher than that of molecular the O₂/H₂O reaction? Answer, a planetary game changer.

Oxygenic Photophosphorylation

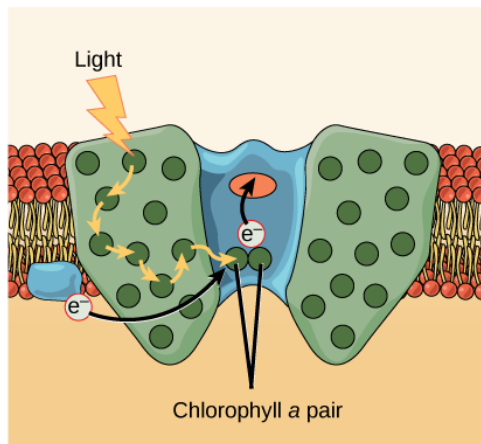
Generation of NADPH and ATP

The overall function of light-dependent reactions is to convert solar energy into chemical energy in the form of NADPH and ATP. This chemical energy supports the light-independent reactions and fuels the assembly of sugar molecules. The light-dependent reactions are depicted in [\[link\]](#). Protein complexes and pigment molecules work together to produce NADPH and ATP.

(a) Photosystem II (P680)



(b) Photosystem I (P700)



A photosystem consists of a light-harvesting complex and a reaction center. Pigments in the light-harvesting complex pass light energy to two special chlorophyll a molecules in the reaction center. The light excites an electron from the chlorophyll a pair, which passes to the primary electron acceptor. The excited electron must then be replaced. In (a) photosystem II, the electron comes from the splitting of water, which releases oxygen as a waste

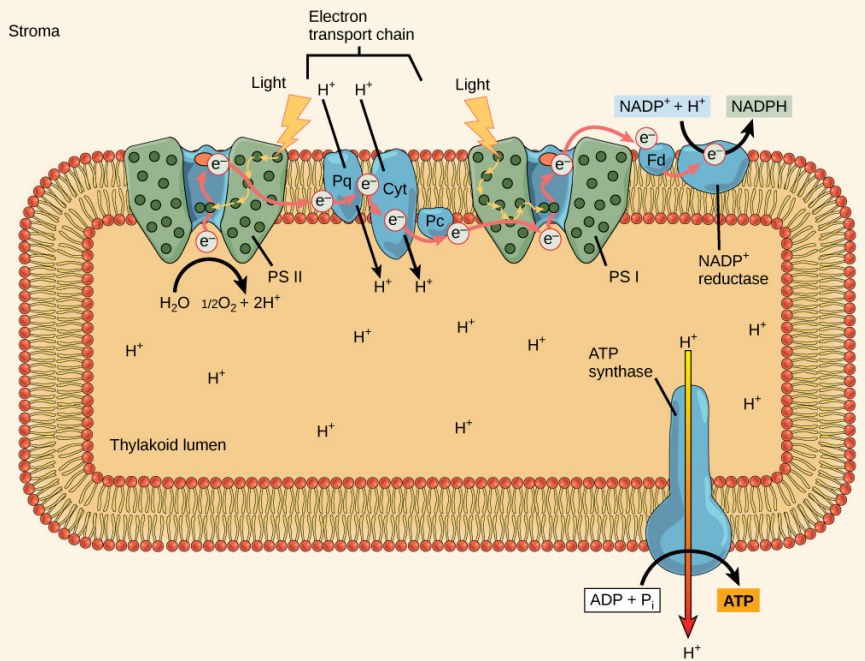
product. In (b) photosystem I, the electron comes from the chloroplast electron transport chain discussed below.

The actual step that converts light energy into chemical energy takes place in a multiprotein complex called a **photosystem**, two types of which are found embedded in the thylakoid membrane, **photosystem II** (PSII) and **photosystem I** (PSI) ([\[link\]](#)). The two complexes differ on the basis of what they oxidize (that is, the source of the low-energy electron supply) and what they reduce (the place to which they deliver their energized electrons).

Both photosystems have the same basic structure; a number of **antenna proteins** to which the chlorophyll molecules are bound surround the **reaction center** where the photochemistry takes place. Each photosystem is serviced by the **light-harvesting complex**, which passes energy from sunlight to the reaction center; it consists of multiple antenna proteins that contain a mixture of 300–400 chlorophyll *a* and *b* molecules as well as other pigments like carotenoids. The absorption of a single **photon** or distinct quantity or “packet” of light by any of the chlorophylls pushes that molecule into an excited state. In short, the light energy has now been captured by biological molecules but is not stored in any useful form yet. The energy is transferred from chlorophyll to chlorophyll until eventually (after about a millionth of a second), it is delivered to the reaction center. Up to this point, only energy has been transferred between molecules, not electrons.

Note:

Art Connection



In the photosystem II (PSII) reaction center, energy from sunlight is used to extract electrons from water. The electrons travel through the chloroplast electron transport chain to photosystem I (PSI), which reduces NADP⁺ to NADPH. The electron transport chain moves protons across the thylakoid membrane into the lumen. At the same time, splitting of water adds protons to the lumen, and reduction of NADPH removes protons from the stroma. The net result is a low pH in the thylakoid lumen, and a high pH in the stroma. ATP synthase uses this electrochemical gradient to make ATP.

What is the initial source of electrons for the chloroplast electron transport chain?

- a. water
- b. oxygen
- c. carbon dioxide

d. NADPH

The reaction center contains a pair of chlorophyll *a* molecules with a special property. Those two chlorophylls can undergo oxidation upon excitation; they can actually give up an electron in a process called a **photoact**. It is at this step in the reaction center, this step in photosynthesis, that light energy is converted into an excited electron. All of the subsequent steps involve getting that electron onto the energy carrier NADPH for delivery to the Calvin cycle where the electron is deposited onto carbon for long-term storage in the form of a carbohydrate. PSII and PSI are two major components of the photosynthetic **electron transport chain**, which also includes the **cytochrome complex**. The cytochrome complex, an enzyme composed of two protein complexes, transfers the electrons from the carrier molecule plastoquinone (Pq) to the protein plastocyanin (Pc), thus enabling both the transfer of protons across the thylakoid membrane and the transfer of electrons from PSII to PSI.

The reaction center of PSII (called **P680**) delivers its high-energy electrons, one at the time, to the **primary electron acceptor**, and through the electron transport chain (Pq to cytochrome complex to plastocyanine) to PSI. P680's missing electron is replaced by extracting a low-energy electron from water; thus, water is split and PSII is re-reduced after every photoact. Splitting one H₂O molecule releases two electrons, two hydrogen atoms, and one atom of oxygen. Splitting two molecules is required to form one molecule of diatomic O₂ gas. About 10 percent of the oxygen is used by mitochondria in the leaf to support oxidative phosphorylation. The remainder escapes to the atmosphere where it is used by aerobic organisms to support respiration.

As electrons move through the proteins that reside between PSII and PSI, they lose energy. That energy is used to move hydrogen atoms from the stromal side of the membrane to the thylakoid lumen. Those hydrogen atoms, plus the ones produced by splitting water, accumulate in the thylakoid lumen and will be used to synthesize ATP in a later step. Because the electrons have lost energy prior to their arrival at PSI, they must be re-energized by PSI, hence, another photon is absorbed by the PSI antenna.

That energy is relayed to the PSI reaction center (called **P700**). P700 is oxidized and sends a high-energy electron to NADP^+ to form NADPH. Thus, PSII captures the energy to create proton gradients to make ATP, and PSI captures the energy to reduce NADP^+ into NADPH. The two photosystems work in concert, in part, to guarantee that the production of NADPH will roughly equal the production of ATP. Other mechanisms exist to fine tune that ratio to exactly match the chloroplast's constantly changing energy needs.

Generating an Energy Carrier: ATP

As in the intermembrane space of the mitochondria during cellular respiration, the buildup of hydrogen ions inside the thylakoid lumen creates a concentration gradient. The passive diffusion of hydrogen ions from high concentration (in the thylakoid lumen) to low concentration (in the stroma) is harnessed to create ATP, just as in the electron transport chain of cellular respiration. The ions build up energy because of diffusion and because they all have the same electrical charge, repelling each other.

To release this energy, hydrogen ions will rush through any opening, similar to water jetting through a hole in a dam. In the thylakoid, that opening is a passage through a specialized protein channel called the ATP synthase. The energy released by the hydrogen ion stream allows ATP synthase to attach a third phosphate group to ADP, which forms a molecule of ATP ([\[link\]](#)). The flow of hydrogen ions through ATP synthase is called chemiosmosis because the ions move from an area of high to an area of low concentration through a semi-permeable structure.

Note:

Link to Learning



Visit this [site](#) and click through the animation to view the process of photosynthesis within a leaf.

Some interesting and informative videos

- [wiley_presents_photosynthesis](#)
- [YouTube_photosynthesis](#)
- [YouTube_photosynthesis_and_electron_tower_usage_by_Dr._Easlon](#)

Section Summary

The pigments of the first part of photosynthesis, the light-dependent reactions, absorb energy from sunlight. A photon strikes the antenna pigments of photosystem II to initiate photosynthesis. The energy travels to the reaction center that contains chlorophyll *a* to the electron transport chain, which pumps hydrogen ions into the thylakoid interior. This action builds up a high concentration of ions. The ions flow through ATP synthase via chemiosmosis to form molecules of ATP, which are used for the formation of sugar molecules in the second stage of photosynthesis. Photosystem I absorbs a second photon, which results in the formation of an NADPH molecule, another energy and reducing power carrier for the light-independent reactions.

Art Connections

Exercise:

Problem:

[\[link\]](#) What is the source of electrons for the chloroplast electron transport chain?

- a. Water
- b. Oxygen
- c. Carbon dioxide
- d. NADPH

Solution:

[\[link\]](#) A.

Review Questions

Exercise:

Problem:

Which of the following structures is *not* a component of a photosystem?

- a. ATP synthase
- b. antenna molecule
- c. reaction center
- d. primary electron acceptor

Solution:

A

Exercise:

Problem:

How many photons does it take to fully reduce one molecule of NADP^+ to NADPH?

- a. 1
- b. 2
- c. 4
- d. 8

Solution:

B

Exercise:**Problem:**

Which complex is *not* involved in the establishment of conditions for ATP synthesis?

- a. photosystem I
- b. ATP synthase
- c. photosystem II
- d. cytochrome complex

Solution:

C

Exercise:**Problem:**

From which component of the light-dependent reactions does NADPH form most directly?

- a. photosystem II

- b. photosystem I
- c. cytochrome complex
- d. ATP synthase

Solution:

B

Free Response

Exercise:

Problem:

Describe the pathway of electron transfer from photosystem II to photosystem I in light-dependent reactions.

Solution:

A photon of light hits an antenna molecule in photosystem II, and the energy released by it travels through other antenna molecules to the reaction center. The energy causes an electron to leave a molecule of chlorophyll *a* to a primary electron acceptor protein. The electron travels through the electron transport chain and is accepted by a pigment molecule in photosystem I.

Exercise:

Problem: What are the roles of ATP and NADPH in photosynthesis?

Solution:

Both of these molecules carry energy; in the case of NADPH, it has reducing power that is used to fuel the process of making carbohydrate molecules in light-independent reactions.

Glossary

absorption spectrum

range of wavelengths of electromagnetic radiation absorbed by a given substance

antenna protein

pigment molecule that directly absorbs light and transfers the energy absorbed to other pigment molecules

carotenoid

photosynthetic pigment that functions to dispose of excess energy

chlorophyll *a*

form of chlorophyll that absorbs violet-blue and red light and consequently has a bluish-green color; the only pigment molecule that performs the photochemistry by getting excited and losing an electron to the electron transport chain

chlorophyll *b*

accessory pigment that absorbs blue and red-orange light and consequently has a yellowish-green tint

cytochrome complex

group of reversibly oxidizable and reducible proteins that forms part of the electron transport chain between photosystem II and photosystem I

electromagnetic spectrum

range of all possible frequencies of radiation

electron transport chain

group of proteins between PSII and PSI that pass energized electrons and use the energy released by the electrons to move hydrogen ions against their concentration gradient into the thylakoid lumen

light harvesting complex

complex that passes energy from sunlight to the reaction center in each photosystem; it consists of multiple antenna proteins that contain a

mixture of 300–400 chlorophyll *a* and *b* molecules as well as other pigments like carotenoids

P680

reaction center of photosystem II

P700

reaction center of photosystem I

photoact

ejection of an electron from a reaction center using the energy of an absorbed photon

photon

distinct quantity or “packet” of light energy

photosystem

group of proteins, chlorophyll, and other pigments that are used in the light-dependent reactions of photosynthesis to absorb light energy and convert it into chemical energy

photosystem I

integral pigment and protein complex in thylakoid membranes that uses light energy to transport electrons from plastocyanin to NADP^+ (which becomes reduced to NADPH in the process)

photosystem II

integral protein and pigment complex in thylakoid membranes that transports electrons from water to the electron transport chain; oxygen is a product of PSII

primary electron acceptor

pigment or other organic molecule in the reaction center that accepts an energized electron from the reaction center

reaction center

complex of chlorophyll molecules and other organic molecules that is assembled around a special pair of chlorophyll molecules and a

primary electron acceptor; capable of undergoing oxidation and reduction

spectrophotometer

instrument that can measure transmitted light and compute the absorption

wavelength

distance between consecutive points of equal position (two crests or two troughs) of a wave in a graphic representation; inversely proportional to the energy of the radiation

Bis2A 06.Appendix A review of Red/Ox reactions

By the end of this section, you will be able to:

- Define three common types of chemical reactions (precipitation, acid-base, and oxidation-reduction)
- Classify chemical reactions as one of these three types given appropriate descriptions or chemical equations
- Identify common acids and bases
- Predict the solubility of common inorganic compounds by using solubility rules
- Compute the oxidation states for elements in compounds

This module is a review and supplemental information

This module is meant as a review to oxidation-reduction reactions, balancing red/ox equations and calculating red/ox states of atoms and simple molecules. In Bis2A, you will not need to balance equations or determine (calculate) the red/ox state of an atom or molecule. However, given a pair of compounds you will have to decide which one is the reduced form and which one is the oxidized form. This module may be of use and is provided as an appendix of sorts to the modules in group 6: Energy.

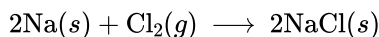
Humans interact with one another in various and complex ways, and we classify these interactions according to common patterns of behavior. When two humans exchange information, we say they are communicating. When they exchange blows with their fists or feet, we say they are fighting. Faced with a wide range of varied interactions between chemical substances, scientists have likewise found it convenient (or even necessary) to classify chemical interactions by identifying common patterns of reactivity. This module will provide an introduction to three of the most prevalent types of chemical reactions: precipitation, acid-base, and oxidation-reduction.

Oxidation-Reduction Reactions

Earth's atmosphere contains about 20% molecular oxygen, O_2 , a chemically reactive gas that plays an essential role in the metabolism of aerobic organisms and in many environmental processes that shape the world. The term **oxidation** was originally used to describe chemical reactions involving O_2 , but its meaning has evolved to refer to a broad and important reaction class known as *oxidation-reduction (redox) reactions*. A few examples of such reactions will be used to develop a clear picture of this classification.

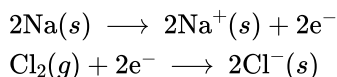
Some redox reactions involve the transfer of electrons between reactant species to yield ionic products, such as the reaction between sodium and chlorine to yield sodium chloride:

Equation:



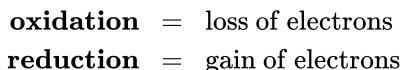
It is helpful to view the process with regard to each individual reactant, that is, to represent the fate of each reactant in the form of an equation called a **half-reaction**:

Equation:



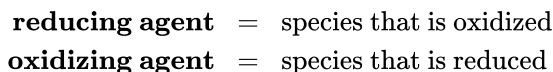
These equations show that Na atoms *lose electrons* while Cl atoms (in the Cl_2 molecule) *gain electrons*, the “s” subscripts for the resulting ions signifying they are present in the form of a solid ionic compound. For redox reactions of this sort, the loss and gain of electrons define the complementary processes that occur:

Equation:



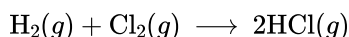
In this reaction, then, sodium is *oxidized* and chlorine undergoes **reduction**. Viewed from a more active perspective, sodium functions as a **reducing agent (reductant)**, since it provides electrons to (or reduces) chlorine. Likewise, chlorine functions as an **oxidizing agent (oxidant)**, as it effectively removes electrons from (oxidizes) sodium.

Equation:



Some redox processes, however, do not involve the transfer of electrons. Consider, for example, a reaction similar to the one yielding NaCl:

Equation:



The product of this reaction is a covalent compound, so transfer of electrons in the explicit sense is not involved. To clarify the similarity of this reaction to the previous one and permit an unambiguous definition of redox reactions, a property called *oxidation number* has been defined. The **oxidation number** (or **oxidation state**) of an element in a compound is the charge its atoms would possess *if the compound was ionic*. The following guidelines are used to assign oxidation numbers to each element in a molecule or ion.

1. The oxidation number of an atom in an elemental substance is zero.
2. The oxidation number of a monatomic ion is equal to the ion's charge.
3. Oxidation numbers for common nonmetals are usually assigned as follows:
 - Hydrogen: +1 when combined with nonmetals, -1 when combined with metals
 - Oxygen: -2 in most compounds, sometimes -1 (so-called peroxides, O_2^{2-}), very rarely $-\frac{1}{2}$ (so-called superoxides, O_2^-), positive values when combined with F (values vary)
 - Halogens: -1 for F always, -1 for other halogens except when combined with oxygen or other halogens (positive oxidation numbers in these cases, varying values)
4. The sum of oxidation numbers for all atoms in a molecule or polyatomic ion equals the charge on the molecule or ion.

Note: The proper convention for reporting charge is to write the number first, followed by the sign (e.g., 2+), while oxidation number is written with the reversed sequence, sign followed by number (e.g., +2). This convention aims to emphasize the distinction between these two related properties.

Example:

Assigning Oxidation Numbers

Follow the guidelines in this section of the text to assign oxidation numbers to all the elements in the following species:

- (a) H_2S
- (b) SO_3^{2-}
- (c) Na_2SO_4

Solution

(a) According to guideline 1, the oxidation number for H is +1.

Using this oxidation number and the compound's formula, guideline 4 may then be used to calculate the oxidation number for sulfur:

Equation:

$$\begin{aligned}\text{charge on H}_2\text{S} = 0 &= (2 \times +1) + (1 \times x) \\ x &= 0 - (2 \times +1) = -2\end{aligned}$$

(b) Guideline 3 suggests the oxidation number for oxygen is -2 .

Using this oxidation number and the ion's formula, guideline 4 may then be used to calculate the oxidation number for sulfur:

Equation:

$$\begin{aligned}\text{charge on SO}_3^{2-} &= -2 = (3 \times -1) + (1 \times x) \\ x &= -2 - (3 \times -1) = +1\end{aligned}$$

(c) For ionic compounds, it's convenient to assign oxidation numbers for the cation and anion separately. According to guideline 2, the oxidation number for sodium is $+1$.

Assuming the usual oxidation number for oxygen (-2 per guideline 3), the oxidation number for sulfur is calculated as directed by guideline 4:

Equation:

$$\begin{aligned}\text{charge on SO}_4^{2-} &= -2 = (4 \times -2) + (1 \times x) \\ x &= -2 - (4 \times -2) = +6\end{aligned}$$

Check Your Learning

Assign oxidation states to the elements whose atoms are underlined in each of the following compounds or ions:

(a) $\text{K}\underline{\text{N}}\text{O}_3$

(b) $\underline{\text{Al}}\text{H}_3$

(c) $\text{N}\underline{\text{H}}_4^+$

(d) $\text{H}_2\underline{\text{P}}\text{O}_4^-$

Note:

Answer:

(a) N, $+5$; (b) Al, $+3$; (c) N, -3 ; (d) P, $+5$

Using the oxidation number concept, an all-inclusive definition of redox reaction has been established. **Oxidation-reduction (redox) reactions** are those in which one or more elements involved undergo a change in oxidation number. (While the vast majority of redox reactions involve changes in oxidation number for two or more elements, a few interesting exceptions to this rule do exist [\[link\]](#).) Definitions for the complementary processes of this reaction class are correspondingly revised as shown here:

Equation:

oxidation = increase in oxidation number

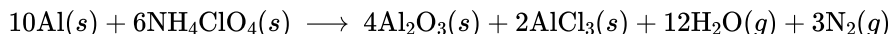
reduction = decrease in oxidation number

Returning to the reactions used to introduce this topic, they may now both be identified as redox processes. In the reaction between sodium and chlorine to yield sodium chloride, sodium is oxidized (its oxidation number increases from 0 in Na to $+1$ in NaCl) and chlorine is reduced (its oxidation number decreases from 0 in Cl_2 to -1 in NaCl). In the reaction between molecular hydrogen and chlorine, hydrogen is oxidized (its oxidation number increases from 0 in H_2 to $+1$ in HCl) and chlorine is reduced (its oxidation number decreases from 0 in Cl_2 to -1 in HCl).

Several subclasses of redox reactions are recognized, including **combustion reactions** in which the reductant (also called a *fuel*) and oxidant (often, but not necessarily, molecular oxygen) react vigorously and produce significant amounts of heat, and often light, in the form of a flame. Solid rocket-fuel reactions such as the one depicted in

[\[link\]](#) are combustion processes. A typical propellant reaction in which solid aluminum is oxidized by ammonium perchlorate is represented by this equation:

Equation:



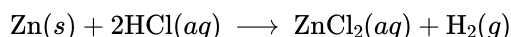
Note:



Watch a brief [video](#) showing the test firing of a small-scale, prototype, hybrid rocket engine planned for use in the new Space Launch System being developed by NASA. The first engines firing at 3 s (green flame) use a liquid fuel/oxidant mixture, and the second, more powerful engines firing at 4 s (yellow flame) use a solid mixture.

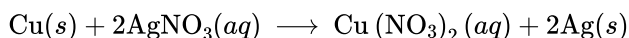
Single-displacement (replacement) reactions are redox reactions in which an ion in solution is displaced (or replaced) via the oxidation of a metallic element. One common example of this type of reaction is the acid oxidation of certain metals:

Equation:

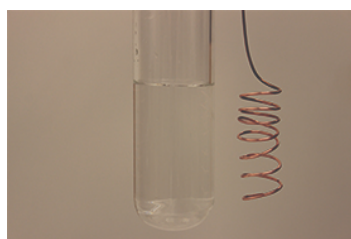


Metallic elements may also be oxidized by solutions of other metal salts; for example:

Equation:



This reaction may be observed by placing copper wire in a solution containing a dissolved silver salt. Silver ions in solution are reduced to elemental silver at the surface of the copper wire, and the resulting Cu^{2+} ions dissolve in the solution to yield a characteristic blue color ([\[link\]](#)).



(a)



(b)



(c)

(a) A copper wire is shown next to a solution containing silver(I) ions. (b) Displacement of dissolved silver ions by copper ions results in (c) accumulation of gray-colored silver metal on the wire and development of a blue color in the solution, due to dissolved copper ions. (credit: modification of work by Mark Ott)

Example:**Describing Redox Reactions**

Identify which equations represent redox reactions, providing a name for the reaction if appropriate. For those reactions identified as redox, name the oxidant and reductant.

- (a) $\text{ZnCO}_3(s) \rightarrow \text{ZnO}(s) + \text{CO}_2(g)$
(b) $2\text{Ga}(l) + 3\text{Br}_2(l) \rightarrow 2\text{GaBr}_3(s)$
(c) $2\text{H}_2\text{O}_2(aq) \rightarrow 2\text{H}_2\text{O}(l) + \text{O}_2(g)$
(d) $\text{BaCl}_2(aq) + \text{K}_2\text{SO}_4(aq) \rightarrow \text{BaSO}_4(s) + 2\text{KCl}(aq)$
(e) $\text{C}_2\text{H}_4(g) + 3\text{O}_2(g) \rightarrow 2\text{CO}_2(g) + 2\text{H}_2\text{O}(l)$

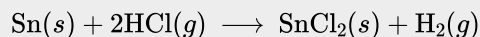
Solution

Redox reactions are identified per definition if one or more elements undergo a change in oxidation number.

- (a) This is not a redox reaction, since oxidation numbers remain unchanged for all elements.
(b) This is a redox reaction. Gallium is oxidized, its oxidation number increasing from 0 in $\text{Ga}(l)$ to +3 in $\text{GaBr}_3(s)$. The reducing agent is $\text{Ga}(l)$. Bromine is reduced, its oxidation number decreasing from 0 in $\text{Br}_2(l)$ to -1 in $\text{GaBr}_3(s)$. The oxidizing agent is $\text{Br}_2(l)$.
(c) This is a redox reaction. It is a particularly interesting process, as it involves the same element, oxygen, undergoing both oxidation and reduction (a so-called *disproportionation reaction*). Oxygen is oxidized, its oxidation number increasing from -1 in $\text{H}_2\text{O}_2(aq)$ to 0 in $\text{O}_2(g)$. Oxygen is also reduced, its oxidation number decreasing from -1 in $\text{H}_2\text{O}_2(aq)$ to -2 in $\text{H}_2\text{O}(l)$. For disproportionation reactions, the same substance functions as an oxidant and a reductant.
(d) This is not a redox reaction, since oxidation numbers remain unchanged for all elements.
(e) This is a redox reaction (combustion). Carbon is oxidized, its oxidation number increasing from -2 in $\text{C}_2\text{H}_4(g)$ to $+4$ in $\text{CO}_2(g)$. The reducing agent (fuel) is $\text{C}_2\text{H}_4(g)$. Oxygen is reduced, its oxidation number decreasing from 0 in $\text{O}_2(g)$ to -2 in $\text{H}_2\text{O}(l)$. The oxidizing agent is $\text{O}_2(g)$.

Check Your Learning

This equation describes the production of tin(II) chloride:

Equation:

Is this a redox reaction? If so, provide a more specific name for the reaction if appropriate, and identify the oxidant and reductant.

Note:**Answer:**

Yes, a single-replacement reaction. $\text{Sn}(s)$ is the reductant, $\text{HCl}(g)$ is the oxidant.

Balancing Redox Reactions via the Half-Reaction Method

Redox reactions that take place in aqueous media often involve water, hydronium ions, and hydroxide ions as reactants or products. Although these species are not oxidized or reduced, they do participate in chemical change in other ways (e.g., by providing the elements required to form oxyanions). Equations representing these reactions are sometimes very difficult to balance by inspection, so systematic approaches have been developed to assist in the process. One very useful approach is to use the method of half-reactions, which involves the following steps:

1. Write the two half-reactions representing the redox process.

2. Balance all elements except oxygen and hydrogen.

3. Balance oxygen atoms by adding H₂O molecules.

4. Balance hydrogen atoms by adding H⁺ ions.

5. Balance charge^[footnote] by adding electrons.

The requirement of “charge balance” is just a specific type of “mass balance” in which the species in question are electrons. An equation must represent equal numbers of electrons on the reactant and product sides, and so both atoms and charges must be balanced.

6. If necessary, multiply each half-reaction’s coefficients by the smallest possible integers to yield equal numbers of electrons in each.

7. Add the balanced half-reactions together and simplify by removing species that appear on both sides of the equation.

8. For reactions occurring in basic media (excess hydroxide ions), carry out these additional steps:

(a) Add OH[−] ions to both sides of the equation in numbers equal to the number of H⁺ ions.

(b) On the side of the equation containing both H⁺ and OH[−] ions, combine these ions to yield water molecules.

(c) Simplify the equation by removing any redundant water molecules.

9. Finally, check to see that both the number of atoms and the total charges^[footnote] are balanced.

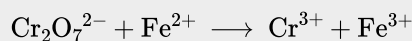
The requirement of “charge balance” is just a specific type of “mass balance” in which the species in question are electrons. An equation must represent equal numbers of electrons on the reactant and product sides, and so both atoms and charges must be balanced.

Example:

Balancing Redox Reactions in Acidic Solution

Write a balanced equation for the reaction between dichromate ion and iron(II) to yield iron(III) and chromium(III) in acidic solution.

Equation:



Solution

Write the Each half-reaction will
two half- contain one reactant and one
reactions. product with one element in
common.

Equation:



Equation:

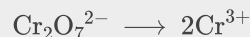


Balance all elements except oxygen and hydrogen. The iron half-reaction is already balanced, but the chromium half-reaction shows two Cr atoms on the left and one Cr atom on the right. Changing the coefficient on the right side of the equation to 2 achieves balance with regard to Cr atoms.

Equation:



Equation:



Balance oxygen atoms by adding H₂O molecules. The iron half-reaction does not contain O atoms. The chromium half-reaction shows seven O atoms on the left and none on the right, so seven water molecules are added to the right side.

Equation:

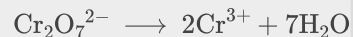


Balance hydrogen atoms by adding H^+ ions. The iron half-reaction does not contain H atoms. The chromium half-reaction shows 14 H atoms on the right and none on the left, so 14 hydrogen ions are added to the left side.

Equation:

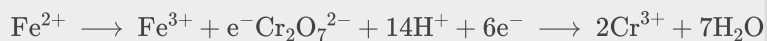


Equation:

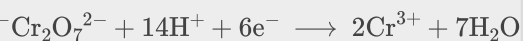


Balance charge by adding electrons. The chromium half-reaction shows a total charge of $(1 \times 2-) + (14 \times 1+) = 12+$ on the left side (1 $\text{Cr}_2\text{O}_7^{2-}$ ion and 14 H^+ ions). The total charge on the right side is $(2 \times 3+) = 6+$ (2 Cr^{3+} ions). Adding six electrons to the right side bring that side's total charge to $(3+) + (1-) = 2+$, to $(12+ + 6-) = 6+$, and charge balance is achieved.

Equation:

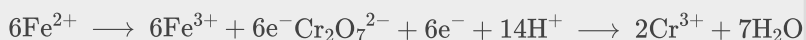


Equation:



Multiply the two half-reactions so the number of electrons in one reaction equals the number of electrons in the other reaction. To be consistent with mass conservation, and the idea that redox reactions involve the transfer (not creation or destruction) of electrons, the iron half-reaction's coefficient must be multiplied by 6.

Equation:



Equation:



Equation:

Add the balanced half-reactions and cancel species that appear on both sides of the equation.



Equation:

Only the six electrons are redundant species. Removing them from each side of the equation yields the simplified, balanced equation here:

A final check of atom and charge balance confirms the equation is balanced.

	Reactants	Products
Fe	6	6
Cr	2	2
O	7	7
H	14	14
charge	24+	24+

Check Your Learning

In acidic solution, hydrogen peroxide reacts with Fe^{2+} to produce Fe^{3+} and H_2O . Write a balanced equation for this reaction.

Note:

Answer:



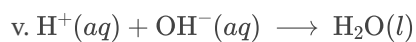
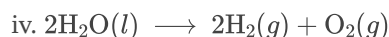
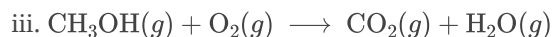
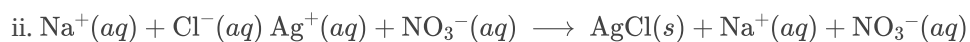
Key Concepts and Summary

Chemical reactions are classified according to similar patterns of behavior. A large number of important reactions are included in three categories: precipitation, acid-base, and oxidation-reduction (redox). Precipitation reactions involve the formation of one or more insoluble products. Acid-base reactions involve the transfer of hydrogen ions between reactants. Redox reactions involve a change in oxidation number for one or more reactant elements. Writing balanced equations for some redox reactions that occur in aqueous solutions is simplified by using a systematic approach called the half-reaction method.

Chemistry End of Chapter Exercises

Exercise:

Problem: Use the following equations to answer the next five questions:



(a) Which equation describes a physical change?

(b) Which equation identifies the reactants and products of a combustion reaction?

(c) Which equation is not balanced?

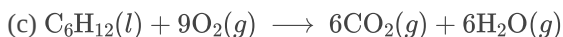
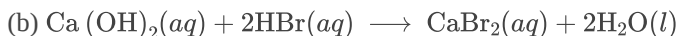
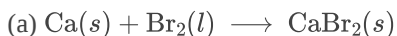
(d) Which is a net ionic equation?

Solution:

(a) i. The transition is from ice to liquid water. (b) iii. Combustion with oxygen generally produces both CO_2 and H_2O . (c) iii. The balanced equation is $2\text{CH}_3\text{OH}(g) + 3\text{O}_2(g) \longrightarrow 2\text{CO}_2(g) + 4\text{H}_2\text{O}(g)$ (d) v. Only reacting ionic species are present.

Exercise:

Problem: Indicate what type, or types, of reaction each of the following represents:

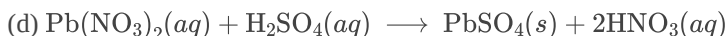
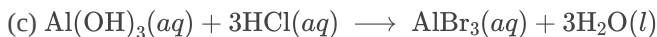
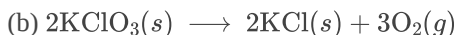
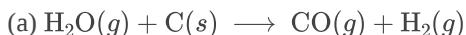


Solution:

(a) oxidation-reduction (addition); (b) acid-base (neutralization); (c) oxidation-reduction (combustion)

Exercise:

Problem: Indicate what type, or types, of reaction each of the following represents:



Solution:

(a) oxidation-reduction (combustion); (b) oxidation-reduction; (c) acid-base (neutralization); (d) precipitation

Exercise:

Problem:

Silver can be separated from gold because silver dissolves in nitric acid while gold does not. Is the dissolution of silver in nitric acid an acid-base reaction or an oxidation-reduction reaction? Explain your answer.

Solution:

An oxidation-reduction reaction, because the oxidation state of the silver changes during the reaction.

Exercise:

Problem: Determine the oxidation states of the elements in the following compounds:



- (c) LiNO_3
 - (d) H_2Se
 - (e) Mg_2Si
 - (f) RbO_2 , rubidium superoxide
 - (g) HF
-

Solution:

- (a) Na +1, I -1; (b) Gd +3, Cl -1; (c) Li +1, N +5, O -2; (d) H +1, Se -2; (e) Mg +2, Si -4; (f) Rb +1; O - $\frac{1}{2}$; (g) H +1, F -1

Exercise:

Problem:

Determine the oxidation states of the elements in the compounds listed. None of the oxygen-containing compounds are peroxides or superoxides.

- (a) H_3PO_4
 - (b) $\text{Al}(\text{OH})_3$
 - (c) SeO_2
 - (d) KNO_2
 - (e) In_2S_3
 - (f) P_4O_6
-

Solution:

- (a) H +1, P +5, O -2; (b) Al +3, H +1, O -2; (c) Se +4, O -2; (d) K +1, N +3, O -2; (e) In +3, S -2; (f) P +3, O -2

Exercise:

Problem:

Determine the oxidation states of the elements in the compounds listed. None of the oxygen-containing compounds are peroxides or superoxides.

- (a) H_2SO_4
 - (b) $\text{Ca}(\text{OH})_2$
 - (c) BrOH
 - (d) ClNO_2
 - (e) TiCl_4
 - (f) NaH
-

Solution:

- (a) H +1, S +6, O -2; (b) Ca +2, O -2, H +1; (c) Br +1, O -2, H +1; (d) Cl +1, N +3, O -2; (e) Ti +4, Cl -1;
(f) Na +1, H -1

Exercise:

Problem: Classify the following as acid-base reactions or oxidation-reduction reactions:

- (a) $\text{Na}_2\text{S}(aq) + 2\text{HCl}(aq) \longrightarrow 2\text{NaCl}(aq) + \text{H}_2\text{S}(g)$
(b) $2\text{Na}(s) + 2\text{HCl}(aq) \longrightarrow 2\text{NaCl}(aq) + \text{H}_2(g)$
(c) $\text{Mg}(s) + \text{Cl}_2(g) \longrightarrow \text{MgCl}_2(s)$
(d) $\text{MgO}(s) + 2\text{HCl}(aq) \longrightarrow \text{MgCl}_2(aq) + \text{H}_2\text{O}(l)$
(e) $\text{K}_3\text{P}(s) + 2\text{O}_2(g) \longrightarrow \text{K}_3\text{PO}_4(s)$
(f) $3\text{KOH}(aq) + \text{H}_3\text{PO}_4(aq) \longrightarrow \text{K}_3\text{PO}_4(aq) + 3\text{H}_2\text{O}(l)$
-

Solution:

(a) acid-base; (b) oxidation-reduction: Na is oxidized, H^+ is reduced; (c) oxidation-reduction: Mg is oxidized, Cl_2 is reduced; (d) acid-base; (e) oxidation-reduction: P^{3-} is oxidized, O_2 is reduced; (f) acid-base

Exercise:

Problem:

Identify the atoms that are oxidized and reduced, the change in oxidation state for each, and the oxidizing and reducing agents in each of the following equations:

- (a) $\text{Mg}(s) + \text{NiCl}_2(aq) \longrightarrow \text{MgCl}_2(aq) + \text{Ni}(s)$
(b) $\text{PCl}_3(l) + \text{Cl}_2(g) \longrightarrow \text{PCl}_5(s)$
(c) $\text{C}_2\text{H}_4(g) + 3\text{O}_2(g) \longrightarrow 2\text{CO}_2(g) + 2\text{H}_2\text{O}(g)$
(d) $\text{Zn}(s) + \text{H}_2\text{SO}_4(aq) \longrightarrow \text{ZnSO}_4(aq) + \text{H}_2(g)$
(e) $2\text{K}_2\text{S}_2\text{O}_3(s) + \text{I}_2(s) \longrightarrow \text{K}_2\text{S}_4\text{O}_6(s) + 2\text{KI}(s)$
(f) $3\text{Cu}(s) + 8\text{HNO}_3(aq) \longrightarrow 3\text{Cu}(\text{NO}_3)_2(aq) + 2\text{NO}(g) + 4\text{H}_2\text{O}(l)$
-

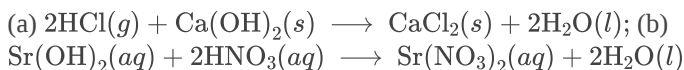
Solution:

(a) Mg is oxidized from 0 to +2 and is the reducing agent, Ni is reduced from +2 to 0 and is the oxidizing agent; (b) P is oxidized from +3 to +5 and is the reducing agent, Cl is reduced from 0 to -1 and is the oxidizing agent; (c) C is oxidized from +2 to +4 and is the reducing agent, O is reduced from 0 to -2 and is the oxidizing agent; (d) Zn is oxidized from 0 to +2 and is the reducing agent, H is reduced from +1 to 0 and is the oxidizing agent; (e) S is oxidized from +2 to +2.5 and is the reducing agent, I_2 is reduced from 0 to -1 and is the oxidizing agent; (f) Cu is oxidized from 0 to +2, N is reduced from +5 to +2

Exercise:

Problem: Complete and balance the following acid-base equations:

- (a) HCl gas reacts with solid $\text{Ca}(\text{OH})_2(s)$.
(b) A solution of $\text{Sr}(\text{OH})_2$ is added to a solution of HNO_3 .
-

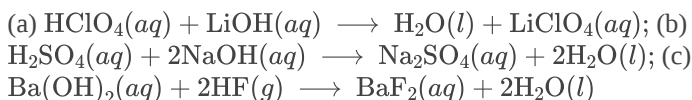
Solution:**Exercise:**

Problem: Complete and balance the following acid-base equations:

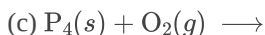
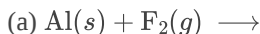
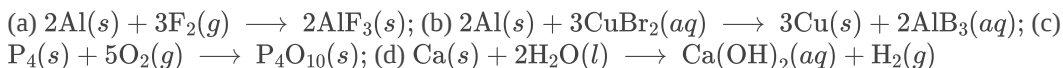
(a) A solution of HClO_4 is added to a solution of LiOH .

(b) Aqueous H_2SO_4 reacts with NaOH .

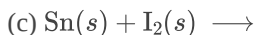
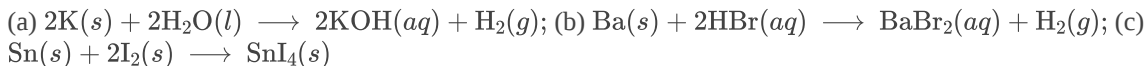
(c) $\text{Ba}(\text{OH})_2$ reacts with HF gas.

Solution:**Exercise:****Problem:**

Complete and balance the following oxidation-reduction reactions, which give the highest possible oxidation state for the oxidized atoms.

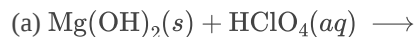
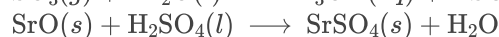
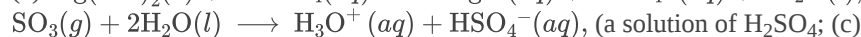
**Solution:****Exercise:****Problem:**

Complete and balance the following oxidation-reduction reactions, which give the highest possible oxidation state for the oxidized atoms.

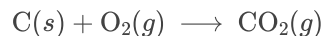
**Solution:****Exercise:**

Problem:

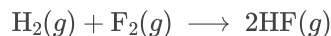
Complete and balance the equations for the following acid-base neutralization reactions. If water is used as a solvent, write the reactants and products as aqueous ions. In some cases, there may be more than one correct answer, depending on the amounts of reactants used.

**Solution:****Exercise:****Problem:**

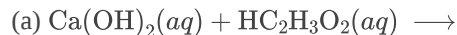
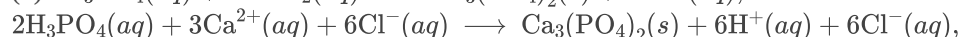
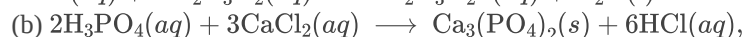
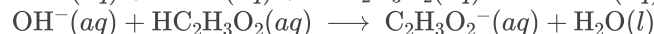
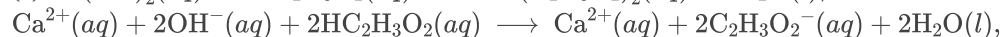
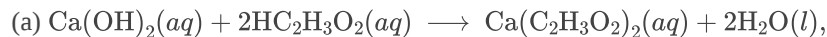
When heated to 700–800 °C, diamonds, which are pure carbon, are oxidized by atmospheric oxygen. (They burn!) Write the balanced equation for this reaction.

Solution:**Exercise:****Problem:**

The military has experimented with lasers that produce very intense light when fluorine combines explosively with hydrogen. What is the balanced equation for this reaction?

Solution:**Exercise:**

Problem: Write the molecular, total ionic, and net ionic equations for the following reactions:

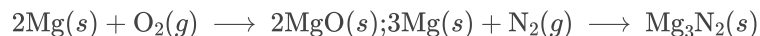
**Solution:****Exercise:**

Problem:

Great Lakes Chemical Company produces bromine, Br₂, from bromide salts such as NaBr, in Arkansas brine by treating the brine with chlorine gas. Write a balanced equation for the reaction of NaBr with Cl₂.

Solution:**Exercise:****Problem:**

In a common experiment in the general chemistry laboratory, magnesium metal is heated in air to produce MgO. MgO is a white solid, but in these experiments it often looks gray, due to small amounts of Mg₃N₂, a compound formed as some of the magnesium reacts with nitrogen. Write a balanced equation for each reaction.

Solution:**Exercise:****Problem:**

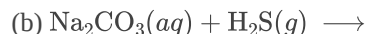
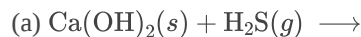
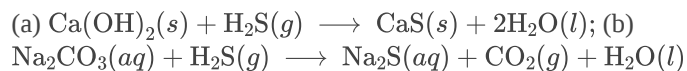
Lithium hydroxide may be used to absorb carbon dioxide in enclosed environments, such as manned spacecraft and submarines. Write an equation for the reaction that involves 2 mol of LiOH per 1 mol of CO₂. (Hint: Water is one of the products.)

Solution:**Exercise:****Problem:**

Calcium propionate is sometimes added to bread to retard spoilage. This compound can be prepared by the reaction of calcium carbonate, CaCO₃, with propionic acid, C₂H₅CO₂H, which has properties similar to those of acetic acid. Write the balanced equation for the formation of calcium propionate.

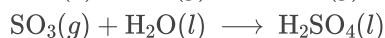
Solution:**Exercise:****Problem:**

Complete and balance the equations of the following reactions, each of which could be used to remove hydrogen sulfide from natural gas:

**Solution:**

Exercise:**Problem:**

Copper(II) sulfide is oxidized by molecular oxygen to produce gaseous sulfur trioxide and solid copper(II) oxide. The gaseous product then reacts with liquid water to produce liquid hydrogen sulfate as the only product. Write the two equations which represent these reactions.

Solution:**Exercise:****Problem:**

Write balanced chemical equations for the reactions used to prepare each of the following compounds from the given starting material(s). In some cases, additional reactants may be required.

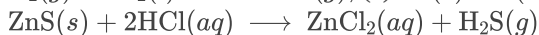
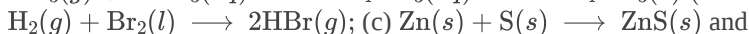
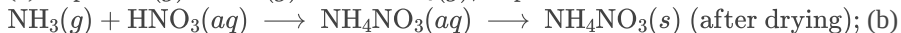
(a) solid ammonium nitrate from gaseous molecular nitrogen via a two-step process (first reduce the nitrogen to ammonia, then neutralize the ammonia with an appropriate acid)

(b) gaseous hydrogen bromide from liquid molecular bromine via a one-step redox reaction

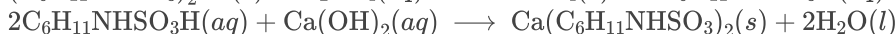
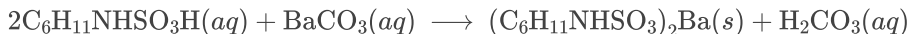
(c) gaseous H_2S from solid Zn and S via a two-step process (first a redox reaction between the starting materials, then reaction of the product with a strong acid)

Solution:

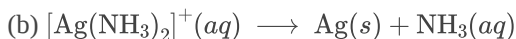
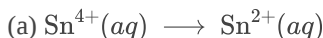
(a) step 1: $\text{N}_2(g) + 3\text{H}_2(g) \longrightarrow 2\text{NH}_3(g)$, step 2:

**Exercise:****Problem:**

Calcium cyclamate $\text{Ca}(\text{C}_6\text{H}_{11}\text{NHSO}_3)_2$ is an artificial sweetener used in many countries around the world but is banned in the United States. It can be purified industrially by converting it to the barium salt through reaction of the acid $\text{C}_6\text{H}_{11}\text{NHSO}_3\text{H}$ with barium carbonate, treatment with sulfuric acid (barium sulfate is very insoluble), and then neutralization with calcium hydroxide. Write the balanced equations for these reactions.

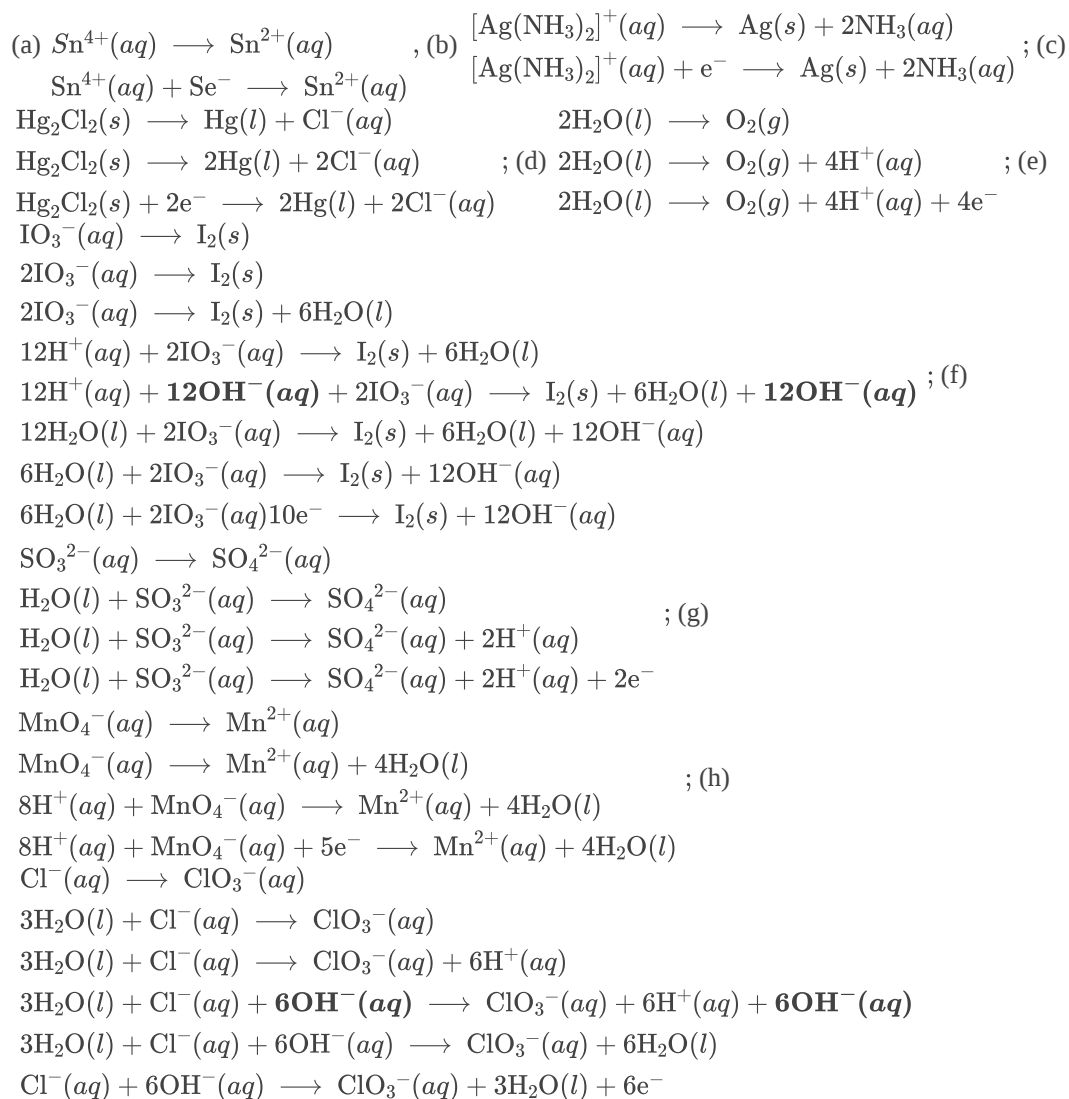
Solution:**Exercise:**

Problem: Complete and balance each of the following half-reactions (steps 2–5 in half-reaction method):



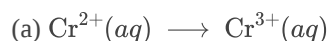
- (c) $\text{Hg}_2\text{Cl}_2(s) \longrightarrow \text{Hg}(l) + \text{Cl}^-(aq)$
- (d) $\text{H}_2\text{O}(l) \longrightarrow \text{O}_2$ (in acidic solution)
- (e) $\text{IO}_3^-(aq) \longrightarrow \text{I}_2(s)$
- (f) $\text{SO}_3^{2-}(aq) \longrightarrow \text{SO}_4^{2-}(aq)$ (in acidic solution)
- (g) $\text{MnO}_4^-(aq) \longrightarrow \text{Mn}^{2+}(aq)$ (in acidic solution)
- (h) $\text{Cl}^-(aq) \longrightarrow \text{ClO}_3^-(aq)$ (in basic solution)

Solution:



Exercise:

Problem: Complete and balance each of the following half-reactions (steps 2–5 in half-reaction method):



- (b) $\text{Hg}(l) + \text{Br}^-(aq) \longrightarrow \text{HgBr}_4^{2-}(aq)$
- (c) $\text{ZnS}(s) \longrightarrow \text{Zn}(s) + \text{S}^{2-}(aq)$
- (d) $\text{H}_2(g) \longrightarrow \text{H}_2\text{O}(l)$ (in basic solution)
- (e) $\text{H}_2(g) \longrightarrow \text{H}_3\text{O}^+(aq)$ (in acidic solution)
- (f) $\text{NO}_3^-(aq) \longrightarrow \text{HNO}_2(aq)$ (in acidic solution)
- (g) $\text{MnO}_2(s) \longrightarrow \text{MnO}_4^-(aq)$ (in basic solution)
- (h) $\text{Cl}^-(aq) \longrightarrow \text{ClO}_3^-(aq)$ (in acidic solution)

Solution:

For an example of the fully worked out solution, see the solution to [\[link\]](#). (a) $\text{Cr}^{2+}(aq) \longrightarrow \text{Cr}^{3+}(aq) + \text{e}^-$; (b) $\text{Hg}(l) + 4\text{Br}^-(aq) \longrightarrow \text{HgBr}_4^{2-}(aq) + 2\text{e}^-$; (c) $\text{ZnS}(s) + 2\text{e}^- \longrightarrow \text{Zn}(s) + \text{S}^{2-}(aq)$; (d) $\text{H}_2(g) + 2\text{OH}^-(aq) \longrightarrow 2\text{H}_2\text{O}(l) + 2\text{e}^-$; (e) $\text{H}_2(g) + 2\text{H}_2\text{O}(l) \longrightarrow 2\text{H}_3\text{O}^+(aq) + 2\text{e}^-$; (f) $\text{NO}_3^-(aq) + 3\text{H}_3\text{O}^+(aq) + 2\text{e}^- \longrightarrow \text{HNO}_2(aq) + 4\text{H}_2\text{O}(l)$; (g) $\text{MnO}_2(s) + 4\text{OH}^-(aq) \longrightarrow \text{MnO}_4^-(aq) + 2\text{H}_2\text{O}(l) + 3\text{e}^-$; (h) $\text{Cl}^-(aq) + 3\text{H}_2\text{O}(l) \longrightarrow \text{ClO}_3^-(aq) + 6\text{H}_3\text{O}^+(aq) + 6\text{e}^-$

Exercise:

Problem: Balance each of the following equations according to the half-reaction method:

- (a) $\text{Sn}^{2+}(aq) + \text{Cu}^{2+}(aq) \longrightarrow \text{Sn}^{4+}(aq) + \text{Cu}^+(aq)$
- (b) $\text{H}_2\text{S}(g) + \text{Hg}_2^{2+}(aq) \longrightarrow \text{Hg}(l) + \text{S}(s)$ (in acid)
- (c) $\text{CN}^-(aq) + \text{ClO}_2(aq) \longrightarrow \text{CNO}^-(aq) + \text{Cl}^-(aq)$ (in acid)
- (d) $\text{Fe}^{2+}(aq) + \text{Ce}^{4+}(aq) \longrightarrow \text{Fe}^{3+}(aq) + \text{Ce}^{3+}(aq)$
- (e) $\text{HBrO}(aq) \longrightarrow \text{Br}^-(aq) + \text{O}_2(g)$ (in acid)

Solution:

For an example of the fully worked out solution, see the solution to [\[link\]](#). (a) $\text{Sn}^{2+}(aq) + 2\text{Cu}^{2+}(aq) \longrightarrow \text{Sn}^{4+}(aq) + 2\text{Cu}^+(aq)$; (b) $\text{H}_2\text{S}(g) + \text{Hg}_2^{2+}(aq) + 2\text{H}_2\text{O}(l) \longrightarrow 2\text{Hg}(l) + \text{S}(s) + 2\text{H}_3\text{O}^+(aq)$; (c) $5\text{CN}^-(aq) + 2\text{ClO}_2(aq) + 3\text{H}_2\text{O}(l) \longrightarrow 5\text{CNO}^-(aq) + 2\text{Cl}^-(aq) + 2\text{H}_3\text{O}^+(aq)$; (d) $\text{Fe}^{2+}(aq) + \text{Ce}^{4+}(aq) \longrightarrow \text{Fe}^{3+}(aq) + \text{Ce}^{3+}(aq)$; (e) $2\text{HBrO}(aq) + 2\text{H}_2\text{O}(l) \longrightarrow 2\text{H}_3\text{O}^+(aq) + 2\text{Br}^-(aq) + \text{O}_2(g)$

Exercise:

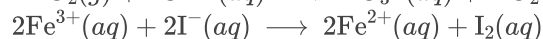
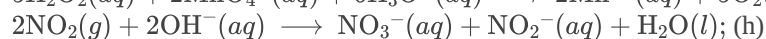
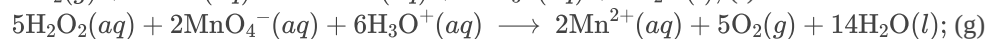
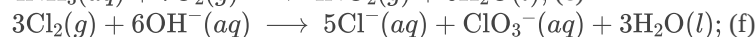
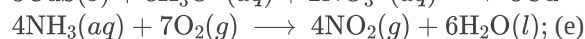
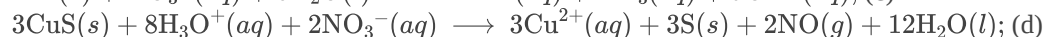
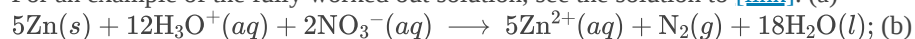
Problem: Balance each of the following equations according to the half-reaction method:

- (a) $\text{Zn}(s) + \text{NO}_3^-(aq) \longrightarrow \text{Zn}^{2+}(aq) + \text{N}_2(g)$ (in acid)
- (b) $\text{Zn}(s) + \text{NO}_3^-(aq) \longrightarrow \text{Zn}^{2+}(aq) + \text{NH}_3(aq)$ (in base)
- (c) $\text{CuS}(s) + \text{NO}_3^-(aq) \longrightarrow \text{Cu}^{2+}(aq) + \text{S}(s) + \text{NO}(g)$ (in acid)

- (d) $\text{NH}_3(aq) + \text{O}_2(g) \longrightarrow \text{NO}_2(g)$ (gas phase)
- (e) $\text{Cl}_2(g) + \text{OH}^-(aq) \longrightarrow \text{Cl}^-(aq) + \text{ClO}_3^-(aq)$ (in base)
- (f) $\text{H}_2\text{O}_2(aq) + \text{MnO}_4^-(aq) \longrightarrow \text{Mn}^{2+}(aq) + \text{O}_2(g)$ (in acid)
- (g) $\text{NO}_2(g) \longrightarrow \text{NO}_3^-(aq) + \text{NO}_2^-(aq)$ (in base)
- (h) $\text{Fe}^{3+}(aq) + \text{I}^-(aq) \longrightarrow \text{Fe}^{2+}(aq) + \text{I}_2(aq)$

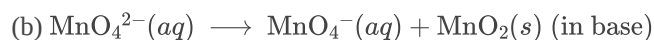
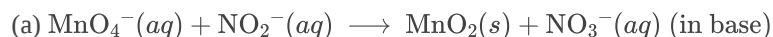
Solution:

For an example of the fully worked out solution, see the solution to [\[link\]](#). (a)



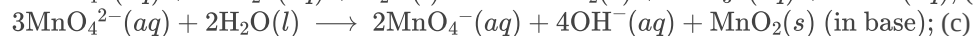
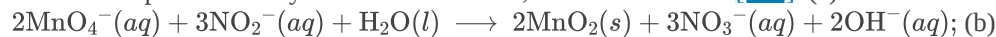
Exercise:

Problem: Balance each of the following equations according to the half-reaction method:



Solution:

For an example of the fully worked out solution, see the solution to [\[link\]](#). (a)



Glossary

acid

substance that produces H_3O^+ when dissolved in water

acid-base reaction

reaction involving the transfer of a hydrogen ion between reactant species

base

substance that produces OH^- when dissolved in water

combustion reaction

vigorous redox reaction producing significant amounts of energy in the form of heat and, sometimes, light

half-reaction

an equation that shows whether each reactant loses or gains electrons in a reaction.

insoluble
of relatively low solubility; dissolving only to a slight extent

neutralization reaction
reaction between an acid and a base to produce salt and water

oxidation
process in which an element's oxidation number is increased by loss of electrons

oxidation-reduction reaction
(also, redox reaction) reaction involving a change in oxidation number for one or more reactant elements

oxidation number
(also, oxidation state) the charge each atom of an element would have in a compound if the compound were ionic

oxidizing agent
(also, oxidant) substance that brings about the oxidation of another substance, and in the process becomes reduced

precipitate
insoluble product that forms from reaction of soluble reactants

precipitation reaction
reaction that produces one or more insoluble products; when reactants are ionic compounds, sometimes called double-displacement or metathesis

reduction
process in which an element's oxidation number is decreased by gain of electrons

reducing agent
(also, reductant) substance that brings about the reduction of another substance, and in the process becomes oxidized

salt
ionic compound that can be formed by the reaction of an acid with a base that contains a cation and an anion other than hydroxide or oxide

single-displacement reaction
(also, replacement) redox reaction involving the oxidation of an elemental substance by an ionic species

soluble
of relatively high solubility; dissolving to a relatively large extent

solubility
the extent to which a substance may be dissolved in water, or any solvent

strong acid
acid that reacts completely when dissolved in water to yield hydronium ions

strong base
base that reacts completely when dissolved in water to yield hydroxide ions

weak acid
acid that reacts only to a slight extent when dissolved in water to yield hydronium ions

weak base
base that reacts only to a slight extent when dissolved in water to yield hydroxide ions

Bis2A 07.1 Glycolysis

By the end of this section, you will be able to:

- Describe the overall result in terms of molecules produced in the breakdown of glucose by glycolysis
- Compare the output of glycolysis in terms of ATP molecules and NADH molecules produced

Introduction to Glycolysis

You are about to begin a series of modules that focus on the oxidation of carbon compounds. This process serves two distinct purposes for any cell. The first is the generation of **metabolic substrates**, small carbon based molecules that all cells need in order to "build" or synthesize larger complexes such as **monomers** which lead to the formation of macromolecules or polymers, such as proteins, or polysaccharides. All cells need twelve (12) basic building blocks or metabolic substrates. In the next few modules we will learn where these metabolic substrates come from and how cells synthesize them. The second purpose is the generation of cellular energy. This can be in the form of ATP (or ATP equivalents) or the formation of **reducing power**. This is primarily in the form of **NADH**, **NADPH** or **FADH₂**.

A note from the instructor as to what is expected of you to know from the reading and lecture

There is a lot of material. I do not expect you to memorize specific names of compounds or enzymes. However, I will give you those names for completeness. For exams I will always provide you with the pathways we discuss in class and in the BioStax Biology text modules. What you need to be able to do is understand what is going on in each reaction. We will go over in lecture, problems that will be similar to those I will ask of you on exams. Do not be overwhelmed with specific enzyme names and specific structures. What you should know are the general types of enzymes used and the types of structures found. For example you do not need to know that the enzyme that converts glyceraldehyde-3-phosphate to 1,3-bisphosphoglycerate is called glyceraldehyde-3-phosphate dehydrogenase. You should know what type of reaction a **dehydrogenase** catalyzes and

while you do not need to memorize the structures of glyceraldehyde-3-phosphate and 1,3-bisphosphoglycerate; you should know that one is an **aldehyde** (is says so in the name) and the other is an **organic acid** (the term "ate" denotes an acid). That is the level of understanding I expect. If you have any questions please ask.

Glycolysis: an overview

So what is glycolysis: it is the process of oxidizing 1 molecule of glucose to 2 pyruvate molecules and the generation of 2 NADH molecules and 2 ATP molecules. Cells can generate cellular energy from the process, 2 ATP molecules are obtained for every molecule of glucose entering the pathway as well as 2 molecules of NADH are generated. In many organism, the oxidation of glucose ends with the generation of pyruvate. For these organisms, for every 1 molecule of glucose oxidized, cells generate only 2 ATP molecules. In other words, these organisms only utilize or extract a small amount of the total potential energy within the glucose molecule. However, for many other organisms, including us humans, the end product pyruvate can be further oxidized by a series of additional reactions, which will be discussed later. In general, these organisms first oxidize pyruvate to acetate or acetyl~CoA, and then the acetyl~CoA is completely oxidized to CO₂ by the **Tricarboxylic acid cycle or TCA cycle**.

In addition to the 2 molecules of ATP and NADH the cells gain a series of small intermediates or precursors that are necessary for the construction of **monomers** which in turn are used to build polymers. These precursors include: **Glucose-6-phosphate, Fructose-6-phosphate, Triose-phosphate, 3-Phosphoglycerate, Phosphoenolpyruvate, and Pyruvate** . These substrates are the building blocks to form monomers that lead to a variety of biopolymers including including proteins (monomer: amino acids) and polysaccharides.

The net result of glycolysis: 2 pyruvates, 2 NADH and 2 ATP. the other important point is that this is an **anaerobic** process. There is no requirement for molecular oxygen in glycolysis. This process occurs in the **cytosol or cytoplasm** of cells. For a short (3 minute) overview YouTube video of glycolysis click [here](#).

Glycolysis: the oxidation of glucose to pyruvate

Glycolysis is the metabolic process of breaking down or oxidizing hexoses, or six carbon sugars, to two molecules of pyruvate, a three carbon keto acid. The importance of glycolysis is really two fold, first is to generate small carbon compounds that the cell can use as building blocks construct other cellular components. Secondly, many cells, including mammals generate energy in form of ATP from glycolysis. While not all cells generate energy from glycolysis, nearly all living organisms carry out glycolysis as part of their metabolism. The process does not use oxygen and is therefore **anaerobic**. Glycolysis takes place in the cytoplasm of bacterial, archeal and eukaryotic cells. Remember that most biological processes are freely reversible, depending upon the needs of the cell. The reverse set of reactions to glycolysis, that is, the process of taking two molecules of pyruvate and reducing them to form one molecule of glucose is called **gluconeogenesis**. The balance between these two process keeps the flux of carbon (hexoses) sensitive to the needs of the cell.

While glycolysis begins with glucose being activated with the addition of a phosphate from ATP, many different types of hexoses (six carbon sugars) and polysaccharides (polymers of sugars) can feed into glycolysis at the point of glucose or glucose-6-phosphate. Many different hexoses, such as Galactose or Mannose, can be converted to glucose by a **hexose isomerase**, an enzyme that can rearrange the hydroxyl groups on the hexose and form glucose. Disaccharides (such as lactose, maltose or sucrose), trisaccharides (such as maltotriose) and polysaccharides (longer sugar polymers such as starch or glycogen) can be degraded by hydrolysis reactions to the monomers which can then be converted to glucose and enter glycolysis. The importance of glycolysis and gluconeogenesis, and along with the TCA cycle is central to all cells for the production of compounds necessary to build the monomers for biopolymers. As a result, these pathways has been given the common name of "**Central Metabolism**".

Glycolysis begins with the six carbon ring-shaped structure of a single glucose molecule and ends with two molecules of a three-carbon sugar called **pyruvate**. Glycolysis consists of two distinct phases. The first part of the glycolysis pathway traps the glucose molecule in the cell and uses

energy to modify it so that the six-carbon sugar molecule can be split evenly into the two three-carbon molecules. The second part of glycolysis extracts energy from the molecules and stores it in the form of ATP and NADH, the reduced form of NAD^+ .

Detailed step by step video of glycolysis

[YouTube presents glycolysis](#)

First Half of Glycolysis (Energy-Requiring Steps)

Step 1. The first step in glycolysis ([\[link\]](#)) is catalyzed by hexokinase, an enzyme with broad specificity that catalyzes the phosphorylation of six-carbon sugars. Hexokinase phosphorylates glucose using ATP as the source of the phosphate, producing glucose-6-phosphate, a more reactive form of glucose. This reaction prevents the phosphorylated glucose molecule from continuing to interact with the GLUT proteins, and it can no longer leave the cell because the negatively charged phosphate will not allow it to cross the hydrophobic interior of the plasma membrane.

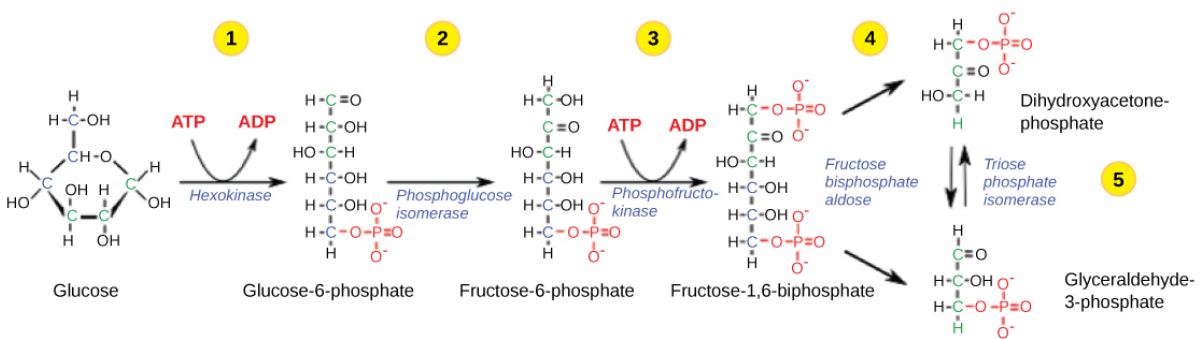
Step 2. In the second step of glycolysis, an isomerase converts glucose-6-phosphate into one of its isomers, fructose-6-phosphate. An **isomerase** is an enzyme that catalyzes the conversion of a molecule into one of its isomers. (This change from phosphoglucose to phosphofructose allows the eventual split of the sugar into two three-carbon molecules.).

Step 3. The third step is the phosphorylation of fructose-6-phosphate, catalyzed by the enzyme phosphofructokinase. A second ATP molecule donates a high-energy phosphate to fructose-6-phosphate, producing fructose-1,6-bisphosphate. In this pathway, phosphofructokinase is a rate-limiting enzyme. It is active when the concentration of ADP is high; it is less active when ADP levels are low and the concentration of ATP is high. Thus, if there is “sufficient” ATP in the system, the pathway slows down. This is a type of end product inhibition, since ATP is the end product of glucose catabolism.

Step 4. The newly added high-energy phosphates further destabilize fructose-1,6-bisphosphate. The fourth step in glycolysis employs an

enzyme, aldolase, to cleave 1,6-bisphosphate into two three-carbon isomers: dihydroxyacetone-phosphate and glyceraldehyde-3-phosphate.

Step 5. In the fifth step, an isomerase transforms the dihydroxyacetone-phosphate into its isomer, glyceraldehyde-3-phosphate. Thus, the pathway will continue with two molecules of a single isomer. At this point in the pathway, there is a net investment of energy from two ATP molecules in the breakdown of one glucose molecule.



The first half of glycolysis uses two ATP molecules in the phosphorylation of glucose, which is then split into two three-carbon molecules.

Exercise: Reading chemical reactions in glycolysis

Problem:

In the first reaction in figure 1. What are the reactants and what are the products?

- Reactants: glucose
- Products: glucose-6-phosphate
- Reactants: glucose and ATP
- Products: ADP and glucose-6-phosphate
- a and b
- c and d

Solution:

f

Exercise:

Problem: The phosphorylation of glucose to glucose 6-phosphate:

- a. Occurs without a catalyst
- b. Is so favorable that the source of phosphate is not important
- c. Is so favorable that it can be used to synthesize ATP
- d. Requires energy from ATP to occur.

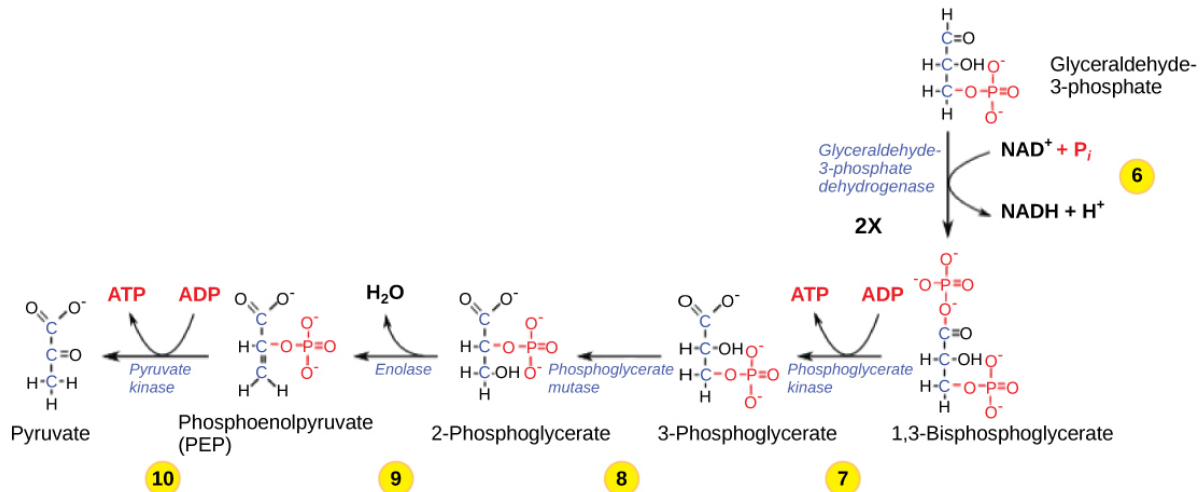
Solution:

d

Second Half of Glycolysis (Energy-Releasing Steps)

So far, glycolysis has cost the cell two ATP molecules and produced two small, three-carbon sugar molecules. Both of these molecules will proceed through the second half of the pathway, and sufficient energy will be extracted to pay back the two ATP molecules used as an initial investment and produce a profit for the cell of two additional ATP molecules and two even higher-energy NADH molecules.

Step 6. The sixth step in glycolysis ([\[link\]](#)) oxidizes the sugar (glyceraldehyde-3-phosphate), extracting high-energy electrons, which are picked up by the electron carrier NAD^+ , producing NADH. The sugar is then phosphorylated by the addition of a second phosphate group, producing 1,3-bisphosphoglycerate. Note that the second phosphate group does not require another ATP molecule.



The second half of glycolysis involves phosphorylation without ATP investment (step 6) and produces two NADH and four ATP molecules per glucose.

Exercise:

Problem:

Which of the following characteristics apply to reaction 6 in figure 2 above?

- This reaction is a redox reaction
- The reactants are NAD, P and G3P
- The products are NADH, H, 13BPG
- Reaction 6 is actually two different, unconnected reactions so it should have two different lists of reactants and two different lists of products.
- a, b, c
- a and d

Solution:

e

Exercise:

Problem:

The energy released by glucose oxidation is captured on _____ and _____.

- a. ATP, NADH
- b. NADH, proton gradient
- c. NAD⁺, ADP
- d. ATP, FADH₂

Solution:

a

Here again is a potential limiting factor for this pathway. The continuation of the reaction depends upon the availability of the oxidized form of the electron carrier, NAD⁺. Thus, NADH must be continuously oxidized back into NAD⁺ in order to keep this step going. If NAD⁺ is not available, the second half of glycolysis slows down or stops. If oxygen is available in the system, the NADH will be oxidized readily, though indirectly, and the high-energy electrons from the hydrogen released in this process will be used to produce ATP. In an environment without oxygen, an alternate pathway (fermentation) can provide the oxidation of NADH to NAD⁺.

Step 7. In the seventh step, catalyzed by phosphoglycerate kinase (an enzyme named for the reverse reaction), 1,3-bisphosphoglycerate donates a high-energy phosphate to ADP, forming one molecule of ATP. (This is an example of substrate-level phosphorylation.) A carbonyl group on the 1,3-bisphosphoglycerate is oxidized to a carboxyl group, and 3-phosphoglycerate is formed.

Step 8. In the eighth step, the remaining phosphate group in 3-phosphoglycerate moves from the third carbon to the second carbon, producing 2-phosphoglycerate (an isomer of 3-phosphoglycerate). The enzyme catalyzing this step is a mutase (isomerase).

Step 9. Enolase catalyzes the ninth step. This enzyme causes 2-phosphoglycerate to lose water from its structure; this is a dehydration reaction, resulting in the formation of a double bond that increases the potential energy in the remaining phosphate bond and produces phosphoenolpyruvate (PEP).

Step 10. The last step in glycolysis is catalyzed by the enzyme pyruvate kinase (the enzyme in this case is named for the reverse reaction of pyruvate's conversion into PEP) and results in the production of a second ATP molecule by substrate-level phosphorylation and the compound pyruvic acid (or its salt form, pyruvate). Many enzymes in enzymatic pathways are named for the reverse reactions, since the enzyme can catalyze both forward and reverse reactions (these may have been described initially by the reverse reaction that takes place in vitro, under non-physiological conditions).

Note:

Link to Learning



Gain a better understanding of the breakdown of glucose by glycolysis by visiting this [site](#) to see the process in action.

Outcomes of Glycolysis

Unfortunately, glycolysis by itself can leave the cell with a problem; how to regenerate NAD^+ from the 2 molecules of NADH produced. If the NAD^+ is not regenerated all of the cell's NAD will be transformed into NADH. This would then cause glycolysis to come to a halt. So how do cells regenerate

NAD^+ , they oxidize the NADH completing the cycle by reducing another compound, usually a small metabolite, such as pyruvate. This process is called **fermentation**. The reduction of pyruvate or another small metabolite leads to the reoxidation of NADH to NAD^+ and the production of a fermentation product such as lactate, acetate, ethanol or some other product. We will discuss fermentation reactions shortly.

The last step in glycolysis is the production of pyruvate. Pyruvate, has a variety of cell fates. In cells that lack an electron transport chain, pyruvate or a breakdown product can act as a terminal electron acceptor in a fermentation reaction necessary to regenerate NAD^+ from the NADH produced during glycolysis. Alternatively, Pyruvate can be oxidized to acetyl~CoA which can then be used as the starting point for the **Tricarboxylic Acid Cycle (TCA Cycle)** or **Krebs Cycle**. This will generate additional ATP (equivalents) NADH and additional precursors necessary for the building of monomers and bio-polymers.

Exercise:

Problem: The flow of carbon through glycolysis can be described as:

- a. Oxidation of a six carbon sugar.
- b. Oxidation of a six carbon sugar, followed by cleavage into two three carbon molecules.
- c. Cleavage of a six carbon sugar into two three carbon molecules, followed by their oxidation.
- d. Conversion of glucose into carbon dioxide.

Solution:

b

Exercise:

Problem: Glycolysis

- a. Does not require oxygen to generate energy.
- b. Requires oxygen to generate energy

- c. Is inhibited by oxygen.
 - d. Rate is increased in the presence of oxygen
-

Solution:

Insert Solution Text Here

Section Summary

Glycolysis is the first pathway used in the breakdown of glucose to extract energy. It was probably one of the earliest metabolic pathways to evolve and is used by nearly all of the organisms on earth. Glycolysis consists of two parts: The first part prepares the six-carbon ring of glucose for cleavage into two three-carbon sugars. ATP is invested in the process during this half to energize the separation. The second half of glycolysis extracts ATP and high-energy electrons from hydrogen atoms and attaches them to NAD^+ . Two ATP molecules are invested in the first half and four ATP molecules are formed by substrate phosphorylation during the second half. This produces a net gain of two ATP and two NADH molecules for the cell.

Review Questions

Exercise:

Problem: During the second half of glycolysis, what occurs?

- a. ATP is used up.
 - b. Fructose is split in two.
 - c. ATP is made.
 - d. Glucose becomes fructose.
-

Solution:

C

Free Response

Exercise:

Problem:

Nearly all organisms on earth carry out some form of glycolysis. How does that fact support or not support the assertion that glycolysis is one of the oldest metabolic pathways?

Solution:

If glycolysis evolved relatively late, it likely would not be as universal in organisms as it is. It probably evolved in very primitive organisms and persisted, with the addition of other pathways of carbohydrate metabolism that evolved later.

Exercise:

Problem:

Red blood cells do not perform aerobic respiration, but they do perform glycolysis. Why do all cells need an energy source, and what would happen if glycolysis were blocked in a red blood cell?

Solution:

All cells must consume energy to carry out basic functions, such as pumping ions across membranes. A red blood cell would lose its membrane potential if glycolysis were blocked, and it would eventually die.

Glossary

aerobic respiration

process in which organisms convert energy in the presence of oxygen

anaerobic

process that does not use oxygen

glycolysis

process of breaking glucose into two three-carbon molecules with the production of ATP and NADH

isomerase

enzyme that converts a molecule into its isomer

pyruvate

three-carbon sugar that can be decarboxylated and oxidized to make acetyl CoA, which enters the citric acid cycle under aerobic conditions; the end product of glycolysis

Bis2A 07.2 Fermentation

By the end of this section, you will be able to:

- Discuss the fundamental difference between anaerobic cellular respiration and fermentation
- Describe the type of fermentation that readily occurs in animal cells and the conditions that initiate that fermentation

FERMENTATION

What happens to the NADH from glycolysis

Exercise:

Thought Question

Problem:

In glycolysis, NAD^+ is converted to NADH; what happens to the NADH produced?

Solution:

Be prepared to discuss this in class.

During glycolysis NAD^+ is reduced to NADH and glucose is oxidized to pyruvate. During this process the cells must regenerate NAD^+ by a second redox reaction. In respiration, this occurs when NADH is used as an electron donor to the electron transport chain. If cells lack an electron transport chain, i.e. can not respire, then cells must use other means to regenerate NAD^+ . This is where fermentation comes into play.

In aerobic respiration, the final electron acceptor is an oxygen molecule, O_2 . If aerobic respiration occurs, then ATP will be produced using the energy of the high-energy electrons carried by NADH or FADH_2 to the electron transport chain. If aerobic respiration does not occur, NADH must be reoxidized to NAD^+ for reuse as an electron carrier for glycolysis to continue. How is this done? Some living systems use an organic molecule

as the final electron acceptor. Processes that use an organic molecule to regenerate NAD^+ from NADH are collectively referred to as **fermentation**.

Helpful videos regarding fermentation

Here is a chemwiki link on [fermentation reactions](#).

Lactic Acid Fermentation

The fermentation method used by animals and some bacteria like those in yogurt is lactic acid fermentation ([link](#)). This occurs routinely in mammalian red blood cells and in skeletal muscle that has insufficient oxygen supply to allow aerobic respiration to continue (that is, in muscles used to the point of fatigue). In muscles, lactic acid produced by fermentation must be removed by the blood circulation and brought to the liver for further metabolism. The chemical reaction of lactic acid fermentation is the following:

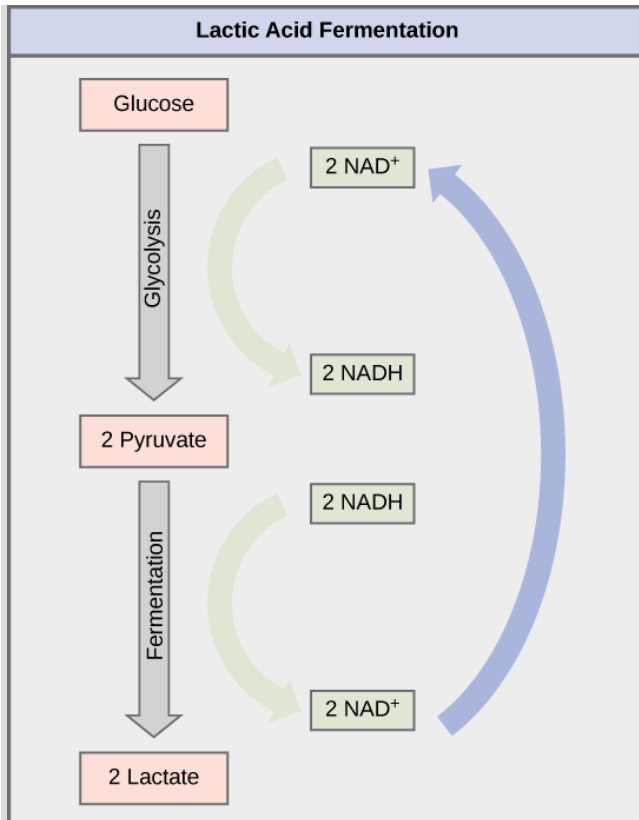
Equation:



The enzyme that catalyzes this reaction is lactate dehydrogenase. The reaction can proceed in either direction, but the left-to-right reaction is inhibited by acidic conditions. This lactic acid build-up causes muscle stiffness and fatigue. Once the lactic acid has been removed from the muscle and is circulated to the liver, it can be converted back to pyruvic acid and further catabolized for energy.

Note:

Art Connection



Lactic acid fermentation is common in muscles that have become exhausted by use.

Exercise:

Problem:

What reactants are used up in glycolysis (need to be replaced)?

- a. NAD⁺
- b. NADH
- c. ATP
- d. ADP
- e. glucose
- f. glycolytic enzymes
- g. a, c and d
- h. a and e

i. all of the above

Solution:

h

Exercise:

Problem:

Which reactants that are used up in glycolysis are "replaced" by the act of fermenting?

- a. NAD⁺
- b. NADH
- c. ATP
- d. ADP
- e. glucose
- f. glycolytic enzymes
- g. a, c and d
- h. a and e
- i. all of the above

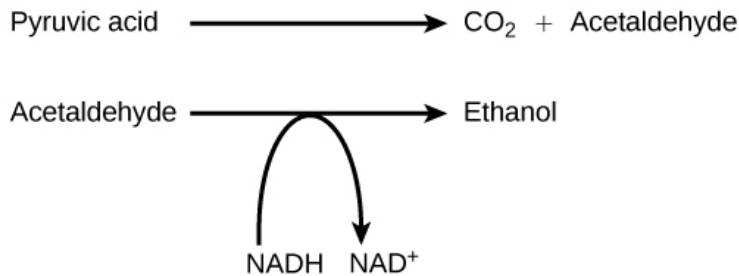
Solution:

a

Tremetol, a metabolic poison found in white snake root plant, prevents the metabolism of lactate. When cows eat this plant, Tremetol is concentrated in the milk. Humans who consume the milk become ill. Symptoms of this disease, which include vomiting, abdominal pain, and tremors, become worse after exercise. Why do you think this is the case?

Alcohol Fermentation

Another familiar fermentation process is alcohol fermentation ([\[link\]](#)), which produces ethanol, an alcohol. The alcohol fermentation reaction is the following:



The reaction resulting in alcohol fermentation is shown.

In the first reaction, a carboxyl group is removed from pyruvic acid, releasing carbon dioxide as a gas. The loss of carbon dioxide reduces the molecule by one carbon atom, making acetaldehyde. The second reaction removes an electron from NADH, forming NAD⁺ and producing ethanol from the acetaldehyde, which accepts the electron. The fermentation of pyruvic acid by yeast produces the ethanol found in alcoholic beverages ([\[link\]](#)). If the carbon dioxide produced by the reaction is not vented from the fermentation chamber, for example in beer and sparkling wines, it remains dissolved in the medium until the pressure is released. Ethanol above 12 percent is toxic to yeast, so natural levels of alcohol in wine occur at a maximum of 12 percent.



Fermentation of grape juice to make wine produces CO_2 as a byproduct. Fermentation tanks have valves so that pressure inside the tanks can be released.

Note:

Concept in Action



Visit this [site](#) to see anaerobic cellular respiration in action.

Other fermentation methods occur in bacteria. Many bacteria are facultatively aerobes. This means that they can switch between aerobic and anaerobic growth depending on the availability of oxygen. Certain bacteria,

like *Clostridia* bacteria, are obligate anaerobes. Obligate anaerobes live and grow in the absence of molecular oxygen. Oxygen is a poison to these microorganisms and kills them upon exposure. It should be noted that many forms of fermentation, an exception is lactic acid fermentation, produce gas, usually CO₂ and acids, such as lactate or acetate. The production of particular types of gas is used as an indicator of the fermentation of specific carbohydrates, which plays a role in the laboratory identification of the bacteria. The various methods of fermentation are used by different organisms to ensure an adequate supply of NAD⁺ for the sixth step in glycolysis. Without these pathways, that step would not occur, and no ATP would be harvested from the breakdown of glucose.

Exercise:

Problem:

Alcohol dehydrogenase in yeast serves the same role as lactate dehydrogenase in mammals. This role is:

- a. To remove excess pyruvate.
- b. To regenerate NAD⁺ from electron transport.
- c. To regenerate NAD⁺ for glycolysis.
- d. To reduce the amount of oxygen needed for growth.

Solution:

c

Additional Links

Here are some additional links to help you study

YouTube

- [Alcohol and lactic acid fermentations](#)

Section Summary

If NADH cannot be metabolized through aerobic respiration, another electron acceptor is used. Most organisms will use some form of fermentation to accomplish the regeneration of NAD^+ , ensuring the continuation of glycolysis. The regeneration of NAD^+ in fermentation is not accompanied by ATP production; therefore, the potential for NADH to produce ATP using an electron transport chain is not utilized.

Art Connections

Exercise:

Problem:

[\[link\]](#) Tremetol, a metabolic poison found in white snake root plant, prevents the metabolism of lactate. When cows eat this plant, Tremetol is concentrated in the milk. Humans who consume the milk become ill. Symptoms of this disease, which include vomiting, abdominal pain, and tremors, become worse after exercise. Why do you think this is the case?

Solution:

[\[link\]](#) The illness is caused by lactic acid build-up. Lactic acid levels rise after exercise, making the symptoms worse. Milk sickness is rare today, but was common in the Midwestern United States in the early 1800s.

Review Questions

Exercise:

Problem:

Which of the following fermentation methods can occur in animal skeletal muscles?

- a. lactic acid fermentation
- b. alcohol fermentation

- c. mixed acid fermentation
 - d. propionic fermentation
-

Solution:

A

Free Response

Exercise:

Problem:

When muscle cells run out of oxygen, what happens to the potential for energy extraction from sugars and what pathways do the cell use?

Solution:

Without oxygen, oxidative phosphorylation and the citric acid cycle stop, so ATP is no longer generated through this mechanism, which extracts the greatest amount of energy from a sugar molecule. In addition, NADH accumulates, preventing glycolysis from going forward because of an absence of NAD^+ . Lactic acid fermentation uses the electrons in NADH to generate lactic acid from pyruvate, which allows glycolysis to continue and thus a smaller amount of ATP can be generated by the cell.

Glossary

fermentation

the steps that follow the partial oxidation of glucose via glycolysis to regenerate NAD^+ ; occurs in the absence of oxygen and uses an organic compound as the final electron acceptor

Bis2A 07.3 Oxidation of Pyruvate and the Citric Acid Cycle

By the end of this section, you will be able to:

- Explain how a circular pathway, such as the citric acid cycle, fundamentally differs from a linear pathway, such as glycolysis
- Describe how pyruvate, the product of glycolysis, is prepared for entry into the citric acid cycle

Introduction to Pyruvate oxidation and the TCA cycle

A Note from the Instructor

As with the module on glycolysis, there is a lot of material in this module. I do not expect you to memorize specific names of compounds or enzymes. However, I will give you those names for completeness. For exams I will always provide you with the pathways we discuss in class and in the BioStax Biology text modules. What you need to be able to do is understand what is going on in each reaction. We will go over in lecture, problems that will be similar to those I will ask of you on exams. Do not be overwhelmed with specific enzyme names and specific structures. What you should know are the general types of enzymes used and the types of structures found. For example you do **not** need to memorize the structures of malate or succinate. You will need to know that both are carboxylic acids if the structure is given to you and should be able to identify the important functional groups. In addition, you will **not** need to know which reactions specifically generate GTP or NADH, but if given the reactions you should be able to tell if a red/ox reaction is occurring. Finally, you will **not** be expected to memorize enzyme names, but like in glycolysis you will be expected to know the various types of reactions a type of enzyme can catalyze, for example, a **dehydrogenase** catalyzes a red/ox reaction. That is the level of understanding I expect. If you have any questions please ask.

Pyruvate oxidation and the TCA cycle

The end-product of glycolysis are 2 pyruvate molecules, 2 ATPs and 2 NADH molecules. The question becomes, what does the cell do with them. ATP can be used for a variety of cellular functions including biosynthesis, transport, replication etc. NADH, is a problem, it needs to be recycled to

NAD⁺. This occurs either through fermentation, in the absence of an electron transport chain, or can be used to generate a proton motive force (PMF) or "energized membrane", which can then lead to either ATP formation or other forms of work (transport of nutrients, cellular locomotion, etc. and will be discussed in later modules). That leaves the cell to deal with pyruvate.

The fate of cellular pyruvate

- Pyruvate can be used as a terminal electron acceptor in fermentation reactions, as was discussed in Module 7.2.
- Pyruvate could be secreted from the cell as a waste product.
- Pyruvate could be further oxidized to extract even more usable cellular energy, which is what will be discussed below.

The further oxidation of pyruvate

The pyruvate formed in glycolysis has a variety of fates depending upon the cell type, physiology and environment the cell is in. In many instances, cells can further oxidize pyruvate, generating additional energy in the form of **GTP** and reducing power, the formation of **NADH (and FADH₂)** along with the production of a variety of additional precursors, which can be used for biosynthesis as required by the cell. In aerobically respiring eukaryotic cells, the pyruvate molecules produced at the end of glycolysis are transported into mitochondria, which are the sites of cellular respiration and house the oxygen consuming electron transport chain. In respiring bacteria and archaea, the pyruvate is further oxidized in the cytoplasm. All three use similar mechanisms to further oxidize the pyruvate to CO₂. Regardless of the organism, if pyruvate is to be further oxidized, the reactions are basically universal: first pyruvate will be transformed into an acetyl group that will be picked up and activated by a carrier compound called **coenzyme A (CoA)** and the resulting **acetyl-CoA** feeds directly into the **Tricarboxylic Acid Cycle** also referred to as the **TCA cycle** or the **Krebs Cycle**. This process is detailed below.

Breakdown of Pyruvate

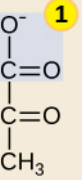
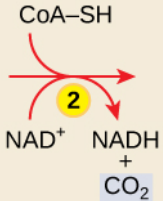
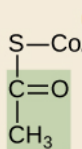
In order for pyruvate, the product of glycolysis, to enter the next pathway, it must undergo several changes. The conversion is a three-step process

([link](#)).

Step 1. A carboxyl group is removed from pyruvate, releasing a molecule of carbon dioxide into the surrounding medium. The result of this step is a two-carbon hydroxyethyl group bound to the enzyme (pyruvate dehydrogenase). This is the first of the six carbons from the original glucose molecule to be removed. This step proceeds twice (remember: there are *two* pyruvate molecules produced at the end of glycolysis) for every molecule of glucose metabolized; thus, two of the six carbons will have been removed at the end of both steps.

Step 2. The hydroxyethyl group is oxidized to an acetyl group, and the electrons are picked up by NAD^+ , forming NADH. The high-energy electrons from NADH will be used later to generate ATP.

Step 3. The enzyme-bound acetyl group is transferred to CoA, producing a molecule of acetyl CoA.

Oxidation of Pyruvate		
 Pyruvate	 Oxidation reaction	 Acetyl CoA
1 A carboxyl group is removed from pyruvate, releasing carbon dioxide.	2 NAD^+ is reduced to NADH.	3 An acetyl group is transferred to coenzyme A, resulting in acetyl CoA.

Upon entering the mitochondrial matrix, a multi-enzyme complex converts pyruvate into acetyl CoA. In the process, carbon dioxide is released

and one molecule of NADH is formed.

Note that during the second stage of glucose metabolism, whenever a carbon atom is removed, it is bound to two oxygen atoms, producing carbon dioxide, one of the major end products of cellular respiration.

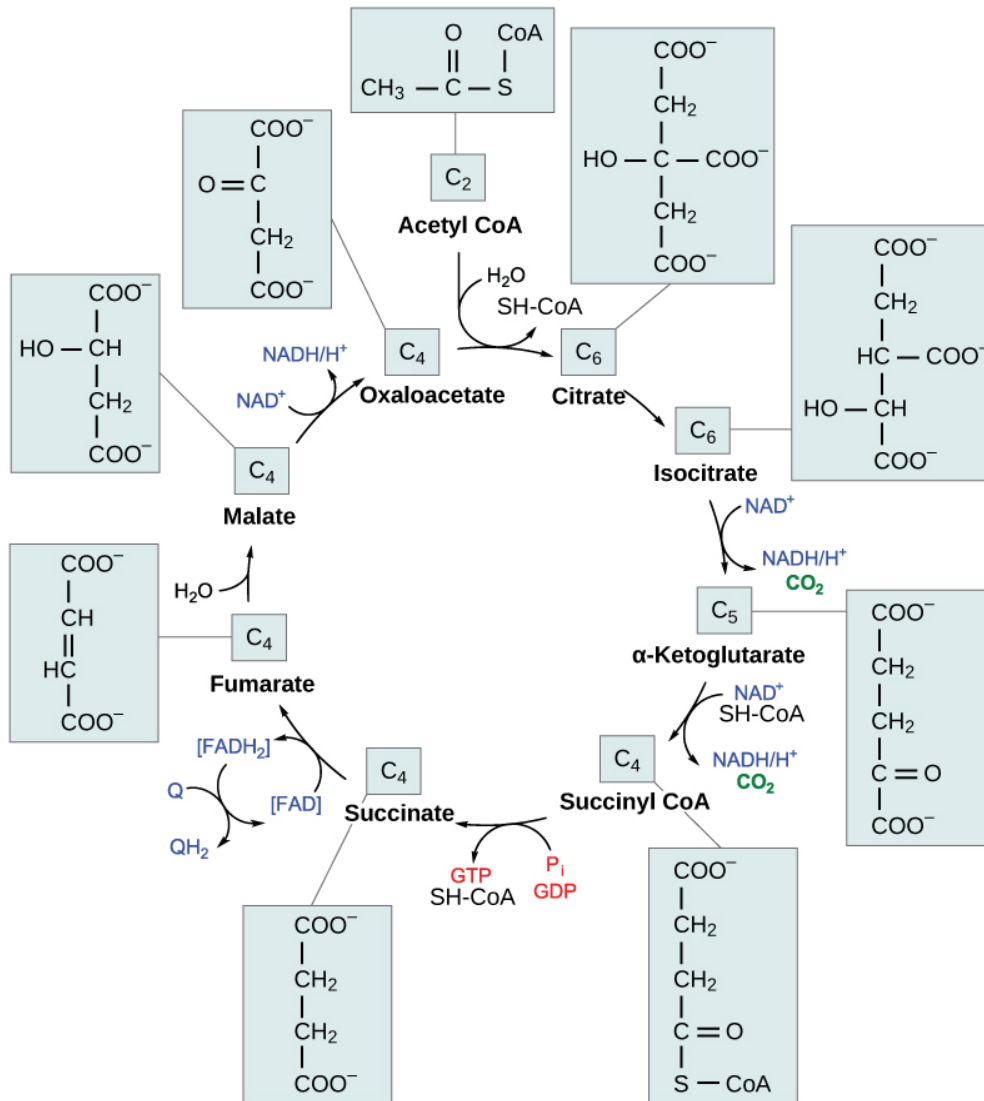
Acetyl CoA to CO₂

In the presence of oxygen, acetyl CoA delivers its acetyl group to a four-carbon molecule, oxaloacetate, to form citrate, a six-carbon molecule with three carboxyl groups; this pathway will harvest the remainder of the extractable energy from what began as a glucose molecule. This single pathway is called by different names: the **citric acid cycle** (for the first intermediate formed—citric acid, or citrate—when acetate joins to the oxaloacetate), the **TCA cycle** (since citric acid or citrate and isocitrate are tricarboxylic acids), and the **Krebs cycle**, after Hans Krebs, who first identified the steps in the pathway in the 1930s in pigeon flight muscles.

Citric Acid Cycle

Like the conversion of pyruvate to acetyl CoA, the citric acid cycle takes place in the matrix of mitochondria. Almost all of the enzymes of the citric acid cycle are soluble, with the single exception of the enzyme succinate dehydrogenase, which is embedded in the inner membrane of the mitochondrion. Unlike glycolysis, the citric acid cycle is a closed loop: The last part of the pathway regenerates the compound used in the first step. The eight steps of the cycle are a series of redox, dehydration, hydration, and decarboxylation reactions that produce two carbon dioxide molecules, one GTP/ATP, and reduced forms of NADH and FADH₂ ([\[link\]](#)). This is considered an aerobic pathway because the NADH and FADH₂ produced must transfer their electrons to the next pathway in the system, which will use oxygen. If this transfer does not occur, the oxidation steps of the citric

acid cycle also do not occur. Note that the citric acid cycle produces very little ATP directly and does not directly consume oxygen.



In the citric acid cycle, the acetyl group from acetyl CoA is attached to a four-carbon oxaloacetate molecule to form a six-carbon citrate molecule. Through a series of steps, citrate is oxidized, releasing two carbon dioxide molecules for each acetyl group fed into the cycle. In the process, three NAD⁺ molecules are reduced to NADH, one FAD molecule is reduced to FADH₂, and one ATP or

GTP (depending on the cell type) is produced (by substrate-level phosphorylation). Because the final product of the citric acid cycle is also the first reactant, the cycle runs continuously in the presence of sufficient reactants. (credit: modification of work by “Yikrazuul”/Wikimedia Commons)

Steps in the Citric Acid Cycle

Step 1. Prior to the start of the first step, a transitional phase occurs during which pyruvic acid is converted to acetyl CoA. Then, the first step of the cycle begins: This is a condensation step, combining the two-carbon acetyl group with a four-carbon oxaloacetate molecule to form a six-carbon molecule of citrate. CoA is bound to a sulfhydryl group (-SH) and diffuses away to eventually combine with another acetyl group. This step is irreversible because it is highly exergonic. The rate of this reaction is controlled by negative feedback and the amount of ATP available. If ATP levels increase, the rate of this reaction decreases. If ATP is in short supply, the rate increases.

Step 2. In step two, citrate loses one water molecule and gains another as citrate is converted into its isomer, isocitrate.

Step 3. In step three, isocitrate is oxidized, producing a five-carbon molecule, α -ketoglutarate, together with a molecule of CO_2 and two electrons, which reduce NAD^+ to NADH. This step is also regulated by negative feedback from ATP and NADH, and a positive effect of ADP.

Steps 3 and 4. Steps three and four are both oxidation and decarboxylation steps, which release electrons that reduce NAD^+ to NADH and release carboxyl groups that form CO_2 molecules. α -Ketoglutarate is the product of step three, and a succinyl group is the product of step four. CoA binds the succinyl group to form succinyl CoA. The enzyme that catalyzes step four is regulated by feedback inhibition of ATP, succinyl CoA, and NADH.

Step 5. In step five, a phosphate group is substituted for coenzyme A, and a high-energy bond is formed. This energy is used in substrate-level phosphorylation (during the conversion of the succinyl group to succinate) to form either guanine triphosphate (GTP) or ATP. There are two forms of the enzyme, called isoenzymes, for this step, depending upon the type of animal tissue in which they are found. One form is found in tissues that use large amounts of ATP, such as heart and skeletal muscle. This form produces ATP. The second form of the enzyme is found in tissues that have a high number of anabolic pathways, such as liver. This form produces GTP. GTP is energetically equivalent to ATP; however, its use is more restricted. In particular, protein synthesis primarily uses GTP.

Step 6. Step six is a dehydration process that converts succinate into fumarate. Two hydrogen atoms are transferred to FAD, producing FADH_2 . The energy contained in the electrons of these atoms is insufficient to reduce NAD^+ but adequate to reduce FAD. Unlike NADH, this carrier remains attached to the enzyme and transfers the electrons to the electron transport chain directly. This process is made possible by the localization of the enzyme catalyzing this step inside the inner membrane of the mitochondrion.

Step 7. Water is added to fumarate during step seven, and malate is produced. The last step in the citric acid cycle regenerates oxaloacetate by oxidizing malate. Another molecule of NADH is produced in the process.

Note:

Link to Learning



Click through each step of the citric acid cycle [here](#).

Products of the Citric Acid Cycle

Two carbon atoms come into the citric acid cycle from each acetyl group, representing four out of the six carbons of one glucose molecule. Two carbon dioxide molecules are released on each turn of the cycle; however, these do not necessarily contain the most recently added carbon atoms. The two acetyl carbon atoms will eventually be released on later turns of the cycle; thus, all six carbon atoms from the original glucose molecule are eventually incorporated into carbon dioxide. Each turn of the cycle forms three NADH molecules and one FADH₂ molecule. These carriers will connect with the last portion of aerobic respiration to produce ATP molecules. One GTP or ATP is also made in each cycle. Several of the intermediate compounds in the citric acid cycle can be used in synthesizing non-essential amino acids; therefore, the cycle is amphibolic (both catabolic and anabolic).

Additional Links

Here are some additional links to videos and pages that you may find useful.

Chemwiki Links

- [Chemwiki TCA cycle](#)

Khan Academy Links

- [Khan Academy TCA cycle](#)

Section Summary

In the presence of oxygen, pyruvate is transformed into an acetyl group attached to a carrier molecule of coenzyme A. The resulting acetyl CoA can enter several pathways, but most often, the acetyl group is delivered to the citric acid cycle for further catabolism. During the conversion of pyruvate into the acetyl group, a molecule of carbon dioxide and two high-energy electrons are removed. The carbon dioxide accounts for two (conversion of two pyruvate molecules) of the six carbons of the original glucose

molecule. The electrons are picked up by NAD^+ , and the NADH carries the electrons to a later pathway for ATP production. At this point, the glucose molecule that originally entered cellular respiration has been completely oxidized. Chemical potential energy stored within the glucose molecule has been transferred to electron carriers or has been used to synthesize a few ATPs.

The citric acid cycle is a series of redox and decarboxylation reactions that remove high-energy electrons and carbon dioxide. The electrons temporarily stored in molecules of NADH and FADH_2 are used to generate ATP in a subsequent pathway. One molecule of either GTP or ATP is produced by substrate-level phosphorylation on each turn of the cycle. There is no comparison of the cyclic pathway with a linear one.

Review Questions

Exercise:

Problem:

What is removed from pyruvate during its conversion into an acetyl group?

- a. oxygen
- b. ATP
- c. B vitamin
- d. carbon dioxide

Solution:

D

Exercise:

Problem: What do the electrons added to NAD^+ do?

- a. They become part of a fermentation pathway.

- b. They go to another pathway for ATP production.
- c. They energize the entry of the acetyl group into the citric acid cycle.
- d. They are converted to NADP.

Solution:

B

Exercise:

Problem: GTP or ATP is produced during the conversion of _____.

- a. isocitrate into α -ketoglutarate
- b. succinyl CoA into succinate
- c. fumarate into malate
- d. malate into oxaloacetate

Solution:

B

Exercise:

Problem:

How many NADH molecules are produced on each turn of the citric acid cycle?

- a. one
- b. two
- c. three
- d. four

Solution:

C

Free Response

Exercise:

Problem:

What is the primary difference between a circular pathway and a linear pathway?

Solution:

In a circular pathway, the final product of the reaction is also the initial reactant. The pathway is self-perpetuating, as long as any of the intermediates of the pathway are supplied. Circular pathways are able to accommodate multiple entry and exit points, thus being particularly well suited for amphibolic pathways. In a linear pathway, one trip through the pathway completes the pathway, and a second trip would be an independent event.

Glossary

acetyl CoA

combination of an acetyl group derived from pyruvic acid and coenzyme A, which is made from pantothenic acid (a B-group vitamin)

citric acid cycle

(also, Krebs cycle) series of enzyme-catalyzed chemical reactions of central importance in all living cells

Krebs cycle

(also, citric acid cycle) alternate name for the citric acid cycle, named after Hans Krebs who first identified the steps in the pathway in the 1930s in pigeon flight muscles; see citric acid cycle

TCA cycle

(also, citric acid cycle) alternate name for the citric acid cycle, named after the group name for citric acid, tricarboxylic acid (TCA); see citric acid cycle

Bis2A 07.4 Pentose Phosphate Pathway

Intro into the Pentose Pathway

In most introductory biology and biochemistry courses focus on glycolysis (oxidation of glucose to pyruvate) and the TCA cycle, the oxidation of pyruvate to acetyl~CoA and the eventual complete oxidation to CO₂. While these are extremely important and universal reactions, most courses leave out the pentose phosphate pathway or hexose monophosphate shunt. This pathway, like the TCA cycle is partially cyclic in nature, where 3 glucose molecules enter and 2 glucose and 1 glyceraldehyde-3-phosphate leave. The 2 glucose molecules can recycle and the G3P enters glycolysis. Its an important pathway because it is the primary mechanism for the formation of pentoses, the five carbon sugar required for nucleotide biosynthesis as well as the formation of a variety of other essential cellular components and NADPH, the cellular reductant primarily used in anabolic reactions.

A note from the Instuctor

As with the modules on glycolysis and the TCA cycle, there is a lot of material in this module. AS with the other modules, I do not expect you to memorize specific names of compounds or enzymes. However, I will give you those names for completeness. For exams I will always provide you with the pathways we discuss in class and in the BioStax Biology text modules. What you need to be able to do is understand what is going on in each reaction. We will go over in lecture, problems that will be similar to those I will ask of you on exams. Do not be overwhelmed with specific enzyme names and specific structures. What you should know are the general types of enzymes used and the types of structures found. For example you do **not** need to memorize the structures of eyrthose or sedoheptulose. You will need to know that both are sugars, the former a 4-carbon sugar and the latter a 7-carbon sugar. Remember the ending "ose" identifies the compound as a sugar. In addition, you will **not** need to know the details of the two unique reactins found in the PPP, the **transketolase** and **transaldolase** reactions, thow you do need to be able to identify a ketone containing sugar versus an aldehyde containing sugar. Finally, you will **not** be expected to memorize enzyme names, but like in glycolysis and the TCA cycle you will be expected to know the various types of reactions

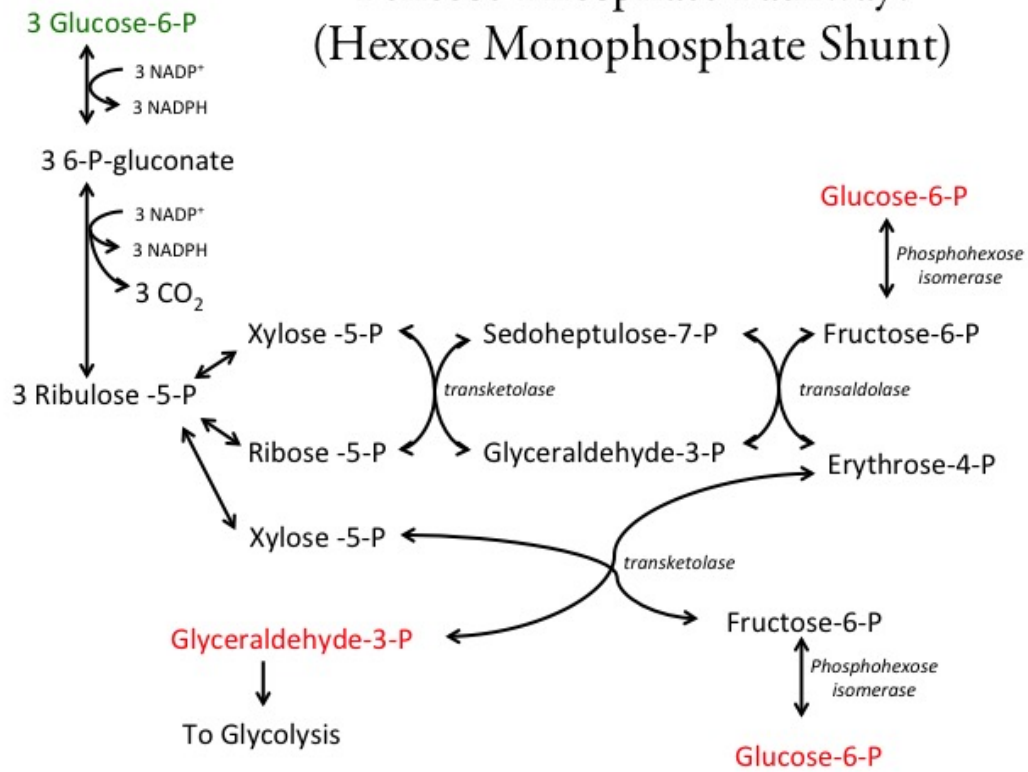
a type of enzyme can catalyze, for example, a **transaldolase** moves aldehyde groups from one compound to another. This is the level of understanding I expect. If you have any questions please ask.

Oxidative Pentose Phosphate Pathway: AKA The hexose monophosphate shunt

While glycolysis has evolved to oxidize hexoses to form carbon precursors for biosynthesis, energy (ATP) and reducing power (NADH) the Pentose Phosphate Pathway (PPP) has evolved to utilize pentoses or five carbon sugars. Pentose are required precursors for nucleotides and other essential biomolecules. The PPP also generates NADPH instead of NADH, which is required for most anabolic reactions. The PPP, in conjunction with Glycolysis and the TCA cycle make up what we call Central Metabolism. These 3 central pathways (along with the reaction Pyruvate to Acetyl~CoA) are responsible for producing all of the necessary precursor molecules required by all cells. The PPP is responsible for producing **pentos-phosphates** (5 carbon sugars), **Erythrose-phosphate**(four carbon sugars)and **NADPH**. This pathway is also responsible for the production of **Sedoheptulose -phosphate**, an essential 7-carbon sugar used in the outer cell membranes of Gram-negative bacteria.

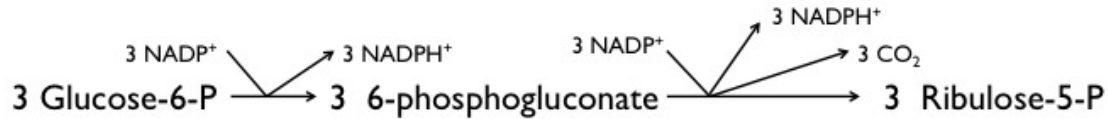
Below is a diagram of the pathway. The pathway is complex and involves a variety of novel rearrangement reactions that move two and three carbon units around. These reactions called **transaldolase** and **transketolase** are used to produce the intermediates within the pathway. The net result is oxidation and subsequent decarboxylation of glucose to form a pentose. The total reaction involves 3 glucose-6-Phosphate (in green) molecules being oxidized to form 3 CO₂ molecules, 1 glyceraldehyde-Phosphate (in red), and 2 hexose-phosphates (in red). In this cycle, the formed glyceraldehyde-Phosphate feeds into glycolysis and the 2 hexose-Phosphates (glucose-Phosphates) can recycle into the PPP or glycolysis.

Pentose Phosphate Pathway: (Hexose Monophosphate Shunt)



Pentose Phosphate Pathway

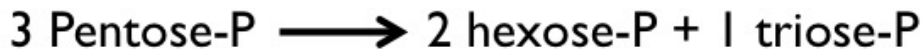
Oxidative reactions



This pathway produces $\text{NADPH} + \text{H}^+$ and pentose-5P
 The reducing power produced is used by anabolic reactions.

The rearrangements

Net reactions from Ribulose-5-P



Singer F2014

1

Take home message

As shown in Figure 2, the net result of the pathway is 1 triose-phosphate (glyceraldehyde-3-Phosphate) that can then be further oxidized via glycolysis; 2 recycled hexose-phosphates (in the form of either glucose-6-phosphate or fructose-6-phosphate) and NADPH which is required reductant for many biosynthetic (anabolic) reactions. The pathway provides a variety of intermediate sugar-phosphates that the cell may require, such as pentose-phosphates (for nucleotides and some amino acids), erythrose-phosphate (for amino acids) and sedohepulose-phosphate, for Gram-negative bacteria.

The PPP along with glycolysis, the TCA cycle and the oxidation of Pyruvate to acetyl-Co makes up the major pathways of central metabolism

and is required to some degree of all organisms to construct the basic substrates to create the building blocks of life.

Section Summary

By the end of this module you should be able to describe the role the pentose phosphate pathway plays in central metabolism. Determine the end-products of the pathway.

Bis2A 07.5 The Calvin Cycle or Using Light Energy to Make Organic Molecules

By the end of this section, you will be able to:

- Describe the Calvin cycle
- Define carbon fixation
- Explain how photosynthesis works in the energy cycle of all living organisms

Intro into Carbon Fixation

The general principle of carbon fixation is that some cells under certain conditions can take inorganic carbon, CO_2 (also referred to as mineralized carbon) and reduce it to a usable cellular form. Most of us are aware that green plants can take up CO_2 and produce O_2 in a process known as photosynthesis. We have already discussed photophosphorylation, the ability of a cell to convert light energy to chemical energy in the form of a high energy electron that then enters the electron transport chain to produce ATP and NADPH, see module as described in Module 6.3. In photosynthesis, the plant cells use the ATP and NADPH formed during photophosphorylation, the light reactions, to reduce CO_2 to sugar, (as we will see, specifically G3P) in what is called the dark reactions. While we all familiar with this process in green plants, I want to point out that this process had its origins in the bacterial world. ATP and NADPH can be made during anoxygenic photophosphorylation and CO_2 into reduced sugars for the cell. In this module we will go over the general reactions of the Calvin Cycle, a reductive pathway that incorporates CO_2 into cellular material. In many ways it is the reverse of the oxidative pentose phosphate pathway. One exercise to keep in mind is to look for the similarities between these two pathways.

A Note from the instructor

As with the modules on glycolysis, the TCA cycle, and the Pentose Phosphate Pathway, there is a lot of material in this module. AS with these other modules, I do not expect you to memorize specific names of compounds or enzymes. However, as in those other modules I will give include the names for completeness. For exams I will always provide you

with the pathways we discuss in class and in the BioStax Biology text modules. What you need to be able to do is understand the underlying principles for each reaction. We will go over in lecture problems that will be similar to those I will ask of you on exams. Do not be overwhelmed with specific enzyme names and specific structures. What you should know are the general types of enzymes used and the types of structures found. If you have any questions please ask.

FIXING CARBON INTO BIOLOGICAL MOLECULES

After the energy from the sun is converted into chemical energy and temporarily stored in ATP and NADPH molecules, the cell has the fuel needed to build carbohydrate molecules for long-term energy storage. The products of the light-dependent reactions, ATP and NADPH, have lifespans in the range of millionths of seconds, whereas the products of the light-independent reactions (carbohydrates and other forms of reduced carbon) can survive for hundreds of millions of years. The carbohydrate molecules made will have a backbone of carbon atoms. Where does the carbon come from? It comes from carbon dioxide, the gas that is a waste product of respiration in microbes, fungi, plants, and animals.

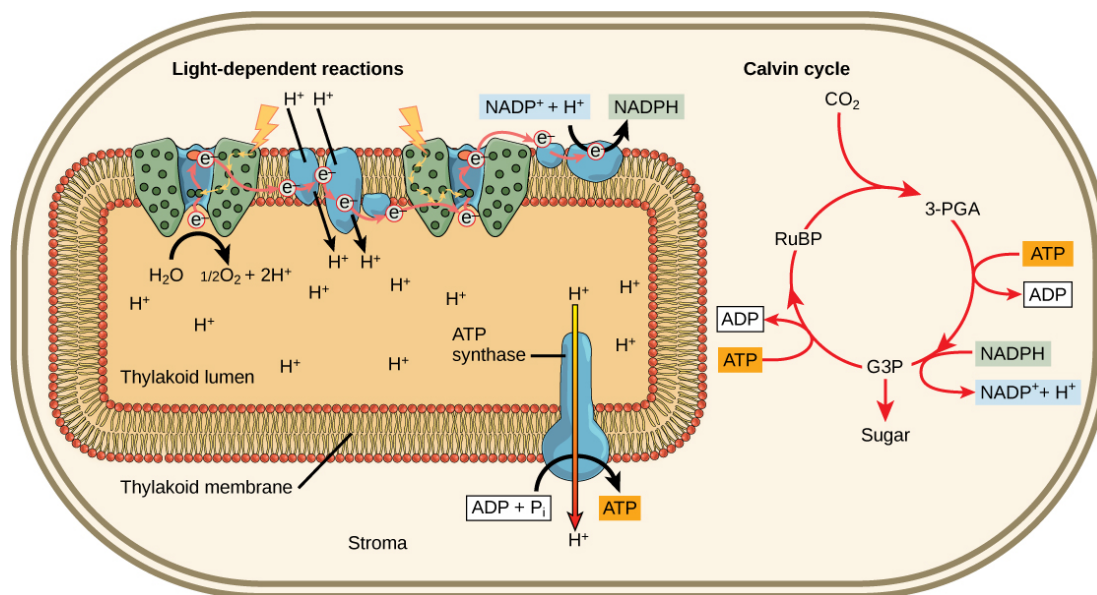
In photosynthetic bacteria, such as Cyanobacteria, and purple non-sulfur bacteria, as well as and plants the energy (ATP) and reducing power (NADPH) obtained from photophosphorylation is coupled to "**Carbon Fixation**", the incorporation of inorganic carbon (CO_2) into organic molecules, glyceraldehyde-3-phosphate (G3P) and eventually into glucose. Organisms that can obtain all of their required carbon from an inorganic source (CO_2) are referred to as **autotrophs**, while those organisms that require organic forms of carbon, such as glucose or protein, are referred to as **heterotrophs**. The biological pathway that leads to carbon fixation is called the **Calvin Cycle** and is a reductive pathway (consumes energy) which leads to the reduction of CO_2 to G3P.

The Calvin Cycle

In plants, carbon dioxide (CO_2) enters the leaves through stomata, where it diffuses over short distances through intercellular spaces until it reaches the

mesophyll cells. Once in the mesophyll cells, CO_2 diffuses into the stroma of the chloroplast—the site of light-independent reactions of photosynthesis. These reactions actually have several names associated with them. Another term, the **Calvin cycle**, is named for the man who discovered it, and because these reactions function as a cycle. Others call it the Calvin-Benson cycle to include the name of another scientist involved in its discovery. The most outdated name is dark reactions, because light is not directly required ([link](#)). However, the term dark reaction can be misleading because it implies incorrectly that the reaction only occurs at night or is independent of light, which is why most scientists and instructors no longer use it.

While the process is similar in bacteria, there are no specific organelles that house the Calvin Cycle genes and the reactions occur in the cytoplasm around a complex membrane system derived from the plasma membrane. This **intracellular membrane system** can be quite complex and highly regulated. In fact, there is strong evidence that supports the hypothesis that the origin of **chloroplasts** comes from a symbiosis between cyanobacteria and early plant cells.



Light reactions harness energy from the sun to produce chemical bonds, ATP, and NADPH. These energy-carrying

molecules are made in the stroma where carbon fixation takes place.

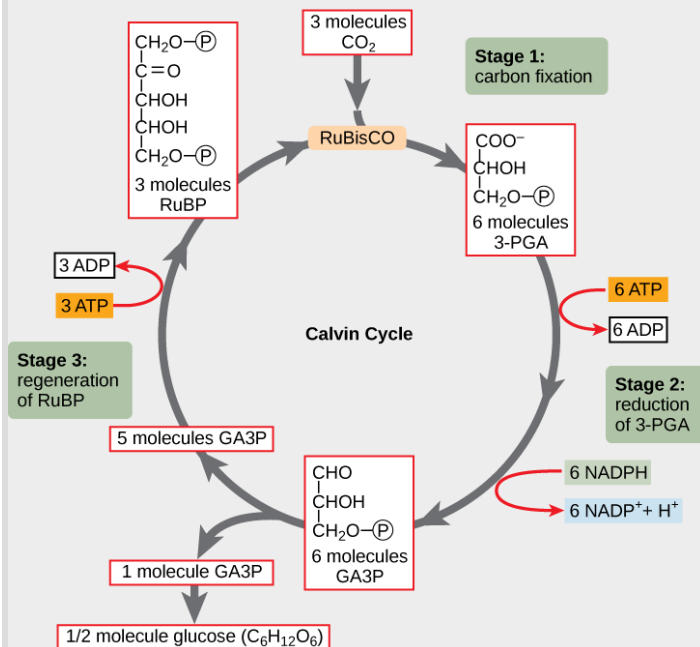
The light-independent reactions of the Calvin cycle can be organized into three basic stages: fixation, reduction, and regeneration.

Stage 1: Fixation

In the stroma of plant chloroplasts, in addition to CO_2 , two other components are present to initiate the light-independent reactions: an enzyme called ribulose-1,5-bisphosphate carboxylase/oxygenase (RuBisCO), and three molecules of ribulose bisphosphate (RuBP), as shown in [\[link\]](#). RuBP has five atoms of carbon, flanked by two phosphates.

Note:

Art Connection



The Calvin cycle has three stages. In

stage 1, the enzyme RuBisCO incorporates carbon dioxide into an organic molecule, 3-PGA. In stage 2, the organic molecule is reduced using electrons supplied by NADPH. In stage 3, RuBP, the molecule that starts the cycle, is regenerated so that the cycle can continue. Only one carbon dioxide molecule is incorporated at a time, so the cycle must be completed three times to produce a single three-carbon GA3P molecule, and six times to produce a six-carbon glucose molecule.

Which of the following statements is true?

- a. In photosynthesis, oxygen, carbon dioxide, ATP, and NADPH are reactants. GA3P and water are products.
- b. In photosynthesis, chlorophyll, water, and carbon dioxide are reactants. GA3P and oxygen are products.
- c. In photosynthesis, water, carbon dioxide, ATP, and NADPH are reactants. RuBP and oxygen are products.
- d. In photosynthesis, water and carbon dioxide are reactants. GA3P and oxygen are products.

RuBisCO catalyzes a reaction between CO_2 and RuBP. For each CO_2 molecule that reacts with one RuBP, two molecules of another compound (3-PGA) form. PGA has three carbons and one phosphate. Each turn of the cycle involves only one RuBP and one carbon dioxide and forms two molecules of 3-PGA. The number of carbon atoms remains the same, as the atoms move to form new bonds during the reactions (3 atoms from 3CO_2 + 15 atoms from 3RuBP = 18 atoms in 3 atoms of 3-PGA). This process is

called **carbon fixation**, because CO_2 is “fixed” from an inorganic form into organic molecules.

Stage 2: Reduction

ATP and NADPH are used to convert the six molecules of 3-PGA into six molecules of a chemical called glyceraldehyde 3-phosphate (G3P). That is a reduction reaction because it involves the gain of electrons by 3-PGA. Recall that a **reduction** is the gain of an electron by an atom or molecule. Six molecules of both ATP and NADPH are used. For ATP, energy is released with the loss of the terminal phosphate atom, converting it into ADP; for NADPH, both energy and a hydrogen atom are lost, converting it into NADP^+ . Both of these molecules return to the nearby light-dependent reactions to be reused and reenergized.

Stage 3: Regeneration

Interestingly, at this point, only one of the G3P molecules leaves the Calvin cycle and is sent to the cytoplasm to contribute to the formation of other compounds needed by the plant. Because the G3P exported from the chloroplast has three carbon atoms, it takes three “turns” of the Calvin cycle to fix enough net carbon to export one G3P. But each turn makes two G3Ps, thus three turns make six G3Ps. One is exported while the remaining five G3P molecules remain in the cycle and are used to regenerate RuBP, which enables the system to prepare for more CO_2 to be fixed. Three more molecules of ATP are used in these regeneration reactions.

Note:

[Link to Learning](#)



This [link](#) leads to an animation of the Calvin cycle. Click stage 1, stage 2, and then stage 3 to see G3P and ATP regenerate to form RuBP.

Note:

Evolution Connection

Photosynthesis

During the evolution of photosynthesis, a major shift occurred from the bacterial type of photosynthesis that involves only one photosystem and is typically anoxygenic (does not generate oxygen) into modern oxygenic (does generate oxygen) photosynthesis, employing two photosystems. This modern oxygenic photosynthesis is used by many organisms—from giant tropical leaves in the rainforest to tiny cyanobacterial cells—and the process and components of this photosynthesis remain largely the same. Photosystems absorb light and use electron transport chains to convert energy into the chemical energy of ATP and NADH. The subsequent light-independent reactions then assemble carbohydrate molecules with this energy.

Photosynthesis in desert plants has evolved adaptations that conserve water. In the harsh dry heat, every drop of water must be used to survive. Because stomata must open to allow for the uptake of CO₂, water escapes from the leaf during active photosynthesis. Desert plants have evolved processes to conserve water and deal with harsh conditions. A more efficient use of CO₂ allows plants to adapt to living with less water. Some plants such as cacti ([link](#)) can prepare materials for photosynthesis during the night by a temporary carbon fixation/storage process, because opening the stomata at this time conserves water due to cooler temperatures. In addition, cacti have evolved the ability to carry out low levels of photosynthesis without opening stomata at all, an extreme mechanism to face extremely dry periods.



The harsh conditions of the desert have led plants like these cacti to evolve variations of the light-independent reactions of photosynthesis. These variations increase the efficiency of water usage, helping to conserve water and energy. (credit: Piotr Wojtkowski)

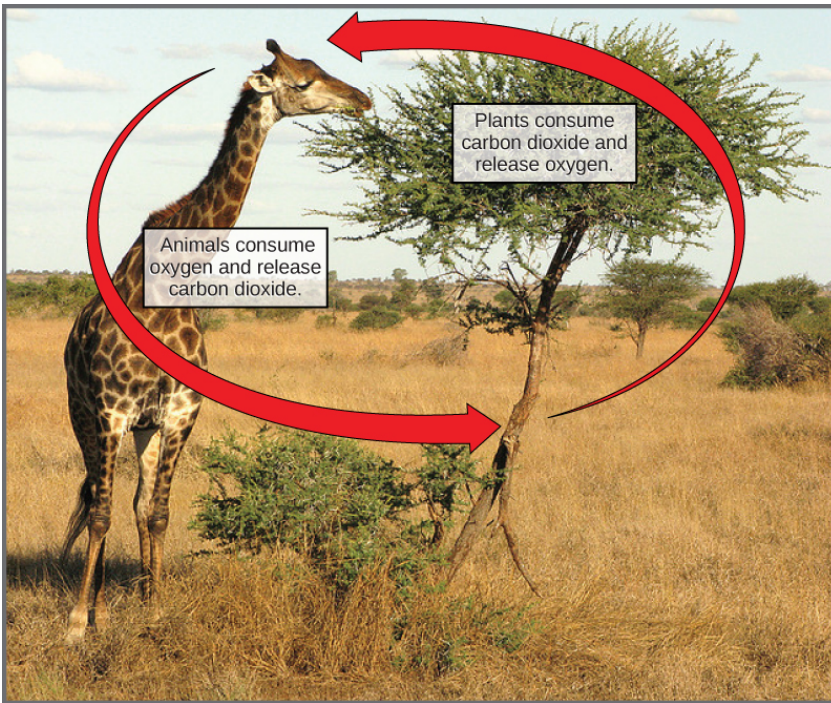
The Energy Cycle

Whether the organism is a bacterium, plant, or animal, all living things access energy by breaking down carbohydrate molecules. But if plants make carbohydrate molecules, why would they need to break them down, especially when it has been shown that the gas organisms release as a “waste product” (CO_2) acts as a substrate for the formation of more food in

photosynthesis? Remember, living things need energy to perform life functions. In addition, an organism can either make its own food or eat another organism—either way, the food still needs to be broken down. Finally, in the process of breaking down food, called cellular respiration, heterotrophs release needed energy and produce “waste” in the form of CO₂ gas.

In nature, there is no such thing as waste. Every single atom of matter and energy is conserved, recycling over and over infinitely. Substances change form or move from one type of molecule to another, but their constituent atoms never disappear ([link](#)).

CO₂ is no more a form of waste than oxygen is wasteful to photosynthesis. Both are byproducts of reactions that move on to other reactions. Photosynthesis absorbs light energy to build carbohydrates in chloroplasts, and aerobic cellular respiration releases energy by using oxygen to metabolize carbohydrates in the cytoplasm and mitochondria. Both processes use electron transport chains to capture the energy necessary to drive other reactions. These two powerhouse processes, photosynthesis and cellular respiration, function in biological, cyclical harmony to allow organisms to access life-sustaining energy that originates millions of miles away in a burning star humans call the sun.



Photosynthesis consumes carbon dioxide and produces oxygen. Aerobic respiration consumes oxygen and produces carbon dioxide. These two processes play an important role in the carbon cycle. (credit: modification of work by Stuart Bassil)

Section Summary

Using the energy carriers formed in the first steps of photosynthesis, the light-independent reactions, or the Calvin cycle, take in CO_2 from the environment. An enzyme, RuBisCO, catalyzes a reaction with CO_2 and another molecule, RuBP. After three cycles, a three-carbon molecule of G3P leaves the cycle to become part of a carbohydrate molecule. The remaining G3P molecules stay in the cycle to be regenerated into RuBP, which is then ready to react with more CO_2 . Photosynthesis forms an energy cycle with the process of cellular respiration. Plants need both photosynthesis and respiration for their ability to function in both the light

and dark, and to be able to interconvert essential metabolites. Therefore, plants contain both chloroplasts and mitochondria.

Additional Links

Khan Academy Links

- [Calvin Cycle](#)

Chemwiki links

- [Calvin Cycle](#)

YouTube Videos

- [3D animation of photosynthesis in plants](#)
- [Calvin Cycle](#)

Art Connections

Exercise:

Problem: [\[link\]](#) Which of the following statements is true?

- In photosynthesis, oxygen, carbon dioxide, ATP, and NADPH are reactants. G3P and water are products.
- In photosynthesis, chlorophyll, water, and carbon dioxide are reactants. G3P and oxygen are products.
- In photosynthesis, water, carbon dioxide, ATP, and NADPH are reactants. RuBP and oxygen are products.
- In photosynthesis, water and carbon dioxide are reactants. G3P and oxygen are products.

Solution:

[\[link\]](#) D

Review Questions

Exercise:

Problem:

Which molecule must enter the Calvin cycle continually for the light-independent reactions to take place?

- a. RuBisCO
- b. RuBP
- c. 3-PGA
- d. CO₂

Solution:

D

Exercise:

Problem:

Which order of molecular conversions is correct for the Calvin cycle?

- a. $\text{RuBP} + \text{G3P} \rightarrow 3\text{-PGA} \rightarrow \text{sugar}$
- b. $\text{RuBisCO} \rightarrow \text{CO}_2 \rightarrow \text{RuBP} \rightarrow \text{G3P}$
- c. $\text{RuBP} + \text{CO}_2 \rightarrow [\text{RuBisCO}] \text{ 3-PGA} \rightarrow \text{G3P}$
- d. $\text{CO}_2 \rightarrow 3\text{-PGA} \rightarrow \text{RuBP} \rightarrow \text{G3P}$

Solution:

C

Exercise:

Problem: Where in eukaryotic cells does the Calvin cycle take place?

- a. thylakoid membrane

- b. thylakoid lumen
- c. chloroplast stroma
- d. granum

Solution:

C

Exercise:

Problem: Which statement correctly describes carbon fixation?

- a. the conversion of CO_2 into an organic compound
- b. the use of RuBisCO to form 3-PGA
- c. the production of carbohydrate molecules from G3P
- d. the formation of RuBP from G3P molecules
- e. the use of ATP and NADPH to reduce CO_2

Solution:

A

Free Response

Exercise:

Problem:

Why is the third stage of the Calvin cycle called the regeneration stage?

Solution:

Because RuBP, the molecule needed at the start of the cycle, is regenerated from G3P.

Exercise:

Problem:

Which part of the light-independent reactions would be affected if a cell could not produce the enzyme RuBisCO?

Solution:

None of the cycle could take place, because RuBisCO is essential in fixing carbon dioxide. Specifically, RuBisCO catalyzes the reaction between carbon dioxide and RuBP at the start of the cycle.

Exercise:**Problem:**

Why does it take three turns of the Calvin cycle to produce G3P, the initial product of photosynthesis?

Solution:

Because G3P has three carbon atoms, and each turn of the cycle takes in one carbon atom in the form of carbon dioxide.

Glossary**Calvin cycle**

light-independent reactions of photosynthesis that convert carbon dioxide from the atmosphere into carbohydrates using the energy and reducing power of ATP and NADPH

carbon fixation

process of converting inorganic CO₂ gas into organic compounds

reduction

gain of electron(s) by an atom or molecule

Bis2A 08.0 Metabolism from a microbes perspective

By the end of this section, you will be able to:

- Identify the macronutrients needed by prokaryotes, and explain their importance
- Describe the ways in which prokaryotes get energy and carbon for life processes
- Describe the roles of prokaryotes in the carbon and nitrogen cycles

METABOLISM: Putting it into perspective

How organisms interact and change with their environment is in essence biology. For simplicity we can start by looking at how the simplest single cell organisms interact and alter their environment and the consequences of those interactions. WE are discussing of course, bacteria and archaea, and we can throw in a simple eukaryote as well. During your reading, think about how cellular activity can change the environment. What does that mean to the environment and the organism.

Bacterial and Archeal metabolism

Bacteria and Archaea are metabolically diverse organisms. There are many different environments on Earth with various energy and carbon sources, and variable conditions. They have been able to live in every environment by using whatever energy and carbon sources are available. Bacteria and Archaea fill many niches on Earth, including being involved in nutrient cycles such as nitrogen and carbon cycles, decomposing dead organisms, and thriving inside living organisms, including humans. The very broad range of environments that bacteria and archaea occupy is possible because they have diverse metabolic processes.

Needs of single cell microbes

The diverse environments and ecosystems on Earth have a wide range of conditions in terms of temperature, available nutrients, acidity, salinity, and energy sources. Prokaryotes are very well equipped to make their living out of a vast array of nutrients and conditions. To live, prokaryotes need a source of energy, a source of carbon, and some additional nutrients.

Macronutrients

Cells are essentially a well-organized assemblage of macromolecules and water. Recall that macromolecules are produced by the polymerization of smaller units called monomers. For cells to build all of the molecules required to sustain life, they need certain substances, collectively called **nutrients**. When prokaryotes grow in nature, they obtain their nutrients from the environment. Nutrients that are required in large amounts are called macronutrients, whereas those required in smaller or trace amounts are called micronutrients. Just a handful of elements are considered macronutrients—carbon, hydrogen, oxygen, nitrogen, phosphorus, and sulfur. (A mnemonic for remembering these elements is the acronym *CHONPS*.)

Why are these macronutrients needed in large amounts? They are the components of organic compounds in cells, including water. Carbon is the major element in all macromolecules: carbohydrates, proteins, nucleic acids, lipids, and many other compounds. Carbon accounts for about 50 percent of the composition of the cell. Nitrogen represents 12 percent of the total dry weight of a typical cell and is a component of proteins, nucleic acids, and other cell constituents. Most of the nitrogen available in nature is either atmospheric nitrogen (N_2) or another inorganic form. Diatomic (N_2) nitrogen, however, can be converted into an organic form only by certain organisms, called nitrogen-fixing organisms. Both hydrogen and oxygen are part of many organic compounds and of water. Phosphorus is required by all organisms for the synthesis of nucleotides and phospholipids. Sulfur is part of the structure of some amino acids such as cysteine and methionine, and is also present in several vitamins and coenzymes. Other important macronutrients are potassium (K), magnesium (Mg), calcium (Ca), and sodium (Na). Although these elements are required in smaller amounts, they are very important for the structure and function of the prokaryotic cell.

Micronutrients

In addition to these macronutrients, bacteria and archaea require various metallic elements in small amounts. These are referred to as micronutrients or trace elements. For example, iron is necessary for the function of the cytochromes involved in electron-transport reactions. Some prokaryotes require other elements—such as boron (B), chromium (Cr), and manganese (Mn)—primarily as enzyme cofactors.

The Ways in Which Bacteria and Archaea Obtain Energy

Bacteria and Archaea can use different sources of energy to assemble macromolecules from smaller molecules. **Phototrophs** (or phototrophic organisms) obtain their energy from sunlight. **Chemotrophs** (or chemosynthetic organisms) obtain their energy from chemical compounds. Chemotrophs that can use organic compounds as energy sources are called chemoorganotrophs. Those that can also use inorganic compounds as energy sources are called chemolithotrophs.

The Ways in Which Bacteria and Archaea Obtain Carbon

Bacteria and Archaea not only can use different sources of energy but also different sources of carbon compounds. Recall that organisms that are able to fix inorganic carbon are called **autotrophs**. Autotrophic organisms synthesize organic molecules from carbon dioxide. In contrast, **heterotrophic** organisms obtain carbon from organic compounds. To make the picture more complex, the terms that describe how organisms obtain energy and carbon can be combined. Thus, photoautotrophs use energy from sunlight, and carbon from carbon dioxide and water, whereas chemoheterotrophs obtain energy and carbon from an organic

chemical source. Chemolithoautotrophs obtain their energy from inorganic compounds, and they build their complex molecules from carbon dioxide. The table below ([link](#)) summarizes carbon and energy sources.

Carbon and Energy Sources in Prokaryotes				
Energy Sources			Carbon Sources	
Light	Chemicals		Carbon dioxide	Organic compounds
Phototrophs	Chemotrophs		Autotrophs	Heterotrophs
	Organic chemicals	Inorganic chemicals		
	Chemo-organotrophs	Chemolithotrophs		

Role of Microbes in Ecosystems

Bacteria and archaea are ubiquitous: There is no niche or ecosystem in which they are not present. They play many roles in the environments they occupy. The roles they play in the carbon and nitrogen cycles are vital to life on Earth.

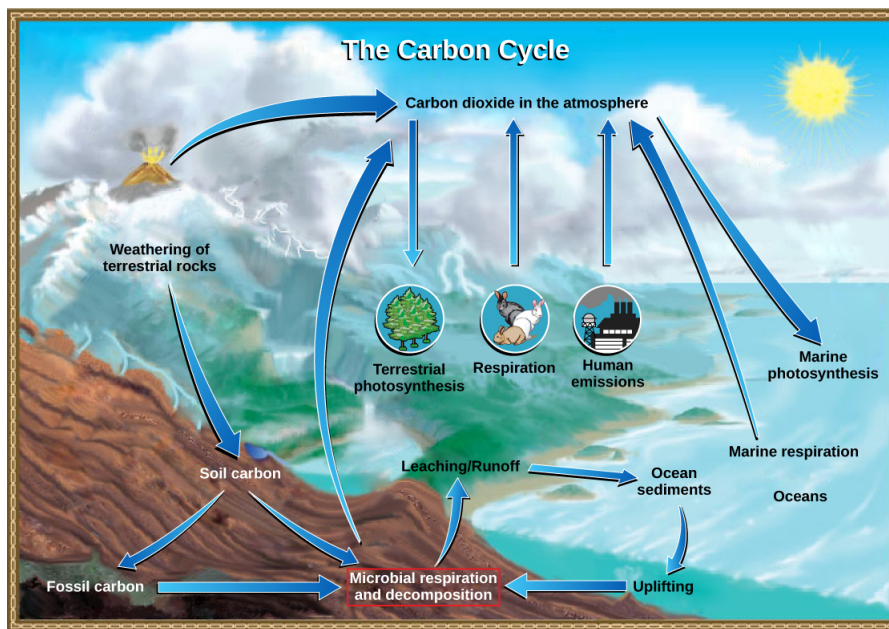
Microbes and the Carbon Cycle

Carbon is one of the most important macronutrients, and prokaryotes play an important role in the carbon cycle ([link](#)). Carbon is cycled through Earth’s major reservoirs: land, the atmosphere, aquatic environments, sediments and rocks, and biomass. The movement of carbon is via carbon dioxide, which is removed from the atmosphere by land plants and marine bacteria, and is returned to the atmosphere via the respiration of chemoorganotrophic organisms, including bacteria, fungi, and animals. Although the largest carbon reservoir in terrestrial ecosystems is in rocks and sediments, that carbon is not readily available.

A large amount of available carbon is found in land plants. Plants, which are producers, use carbon dioxide from the air to synthesize carbon compounds. Related to this, one very significant source of carbon compounds is humus, which is a mixture of organic materials from dead plants and prokaryotes that have resisted decomposition. Consumers such as

animals use organic compounds generated by producers and release carbon dioxide to the atmosphere. Then, bacteria and fungi, collectively called **decomposers**, carry out the breakdown (decomposition) of plants and animals and their organic compounds. The most important contributor of carbon dioxide to the atmosphere is microbial decomposition of dead material (dead animals, plants, and humus) that undergo respiration.

In aqueous environments and their anoxic sediments, there is another carbon cycle taking place. In this case, the cycle is based on one-carbon compounds. In anoxic sediments, archaea produce methane (CH_4). This methane moves into the zone above the sediment, which is richer in oxygen and supports bacteria called methane oxidizers that oxidize methane to carbon dioxide, which then returns to the atmosphere.



Prokaryotes play a significant role in continuously moving carbon through the biosphere. (credit: modification of work by John M. Evans and Howard Perlman, USGS)

Bacteria and the Nitrogen Cycle

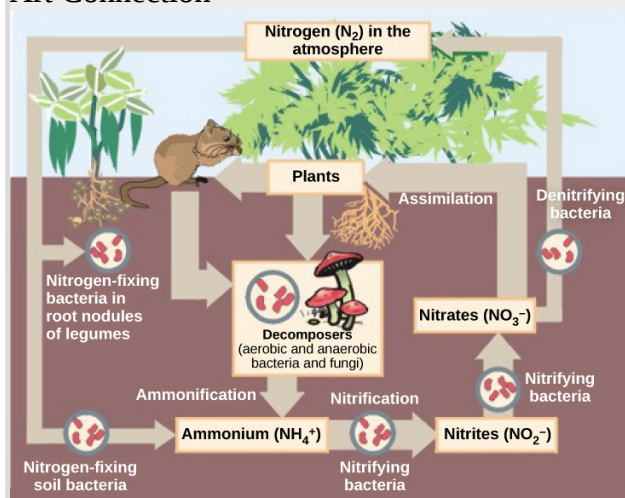
Nitrogen is a very important element for life because it is part of proteins and nucleic acids. It is a macronutrient, and in nature, it is recycled from organic compounds to ammonia, ammonium ions, nitrate, nitrite, and nitrogen gas by myriad processes, many of which are carried out only by prokaryotes. As illustrated in [\[link\]](#), prokaryotes are key to the nitrogen cycle. The largest pool of nitrogen available in the terrestrial ecosystem is gaseous nitrogen

from the air, but this nitrogen is not usable by plants, which are primary producers. Gaseous nitrogen is transformed, or “fixed” into more readily available forms such as ammonia through the process of **nitrogen fixation**. Ammonia can be used by plants or converted to other forms.

Another source of ammonia is **ammonification**, the process by which ammonia is released during the decomposition of nitrogen-containing organic compounds. Ammonia released to the atmosphere, however, represents only 15 percent of the total nitrogen released; the rest is as N_2 and N_2O . Ammonia is catabolized anaerobically by some prokaryotes, yielding N_2 as the final product. **Nitrification** is the conversion of ammonium to nitrite and nitrate. Nitrification in soils is carried out by bacteria belonging to the genera *Nitrosomas*, *Nitrobacter*, and *Nitrospira*. The bacteria performs the reverse process, the reduction of nitrate from the soils to gaseous compounds such as N_2O , NO , and N_2 , a process called **denitrification**.

Note:

Art Connection



Prokaryotes play a key role in the nitrogen cycle. (credit: Environmental Protection Agency)

Which of the following statements about the nitrogen cycle is false?

- a. Nitrogen fixing bacteria exist on the root nodules of legumes and in the soil.
- b. Denitrifying bacteria convert nitrates (NO_3^-) into nitrogen gas (N_2).
- c. Ammonification is the process by which ammonium ion (NH_4^+) is released from decomposing organic compounds.
- d. Nitrification is the process by which nitrites (NO_2^-) are converted to ammonium ion (NH_4^+).

Section Summary

Prokaryotes are the most metabolically diverse organisms; they flourish in many different environments with various carbon energy and carbon sources, variable temperature, pH, pressure, and water availability. Nutrients required in large amounts are called macronutrients, whereas those required in trace amounts are called micronutrients or trace elements. Macronutrients include C, H, O, N, P, S, K, Mg, Ca, and Na. In addition to these macronutrients, prokaryotes require various metallic elements for growth and enzyme function. Prokaryotes use different sources of energy to assemble macromolecules from smaller molecules. Phototrophs obtain their energy from sunlight, whereas chemotrophs obtain energy from chemical compounds.

Prokaryotes play roles in the carbon and nitrogen cycles. Carbon is returned to the atmosphere by the respiration of animals and other chemoorganotrophic organisms. Consumers use organic compounds generated by producers and release carbon dioxide into the atmosphere. The most important contributor of carbon dioxide to the atmosphere is microbial decomposition of dead material. Nitrogen is recycled in nature from organic compounds to ammonia, ammonium ions, nitrite, nitrate, and nitrogen gas. Gaseous nitrogen is transformed into ammonia through nitrogen fixation. Ammonia is anaerobically catabolized by some prokaryotes, yielding N_2 as the final product. Nitrification is the conversion of ammonium into nitrite. Nitrification in soils is carried out by bacteria. Denitrification is also performed by bacteria and transforms nitrate from soils into gaseous nitrogen compounds, such as N_2O , NO , and N_2 .

Art Connections

Exercise:

Problem: [\[link\]](#) Which of the following statements about the nitrogen cycle is false?

- a. Nitrogen fixing bacteria exist on the root nodules of legumes and in the soil.
- b. Denitrifying bacteria convert nitrates (NO_3^-) into nitrogen gas (N_2).
- c. Ammonification is the process by which ammonium ion (NH_4^+) is released from decomposing organic compounds.
- d. Nitrification is the process by which nitrites (NO_2^-) are converted to ammonium ion (NH_4^+).

Solution:

[\[link\]](#) D

Review Questions

Exercise:

Problem: Which of the following elements is *not* a micronutrient?

- a. boron
- b. calcium
- c. chromium
- d. manganese

Solution:

B

Exercise:

Problem:

Prokaryotes that obtain their energy from chemical compounds are called _____.

- a. phototrophs
- b. auxotrophs
- c. chemotrophs
- d. lithotrophs

Solution:

C

Exercise:

Problem: Ammonification is the process by which _____.

- a. ammonia is released during the decomposition of nitrogen-containing organic compounds
- b. ammonium is converted to nitrite and nitrate in soils
- c. nitrate from soil is transformed to gaseous nitrogen compounds such as NO, N₂O, and N₂
- d. gaseous nitrogen is fixed to yield ammonia

Solution:

A

Exercise:

Problem: Plants use carbon dioxide from the air and are therefore called _____.

- a. consumers
- b. producers
- c. decomposer
- d. carbon fixers

Solution:

B

Free Response

Exercise:

Problem:

Think about the conditions (temperature, light, pressure, and organic and inorganic materials) that you may find in a deep-sea hydrothermal vent. What type of prokaryotes, in terms of their metabolic needs (autotrophs, phototrophs, chemotrophs, etc.), would you expect to find there?

Solution:

Responses will vary. In a deep-sea hydrothermal vent, there is no light, so prokaryotes would be chemotrophs instead of phototrophs. The source of carbon would be carbon dioxide dissolved in the ocean, so they would be autotrophs. There is not a lot of organic material in the ocean, so prokaryotes would probably use inorganic sources, thus they would be chemolithotrophs. The temperatures are very high in the hydrothermal vent, so the prokaryotes would be thermophilic.

Glossary

ammonification

process by which ammonia is released during the decomposition of nitrogen-containing organic compounds

chemotroph

organism that obtains energy from chemical compounds

decomposer

organism that carries out the decomposition of dead organisms

denitrification

transformation of nitrate from soil to gaseous nitrogen compounds such as N_2O , NO and N_2

nitrification

conversion of ammonium into nitrite and nitrate in soils

nitrogen fixation

process by which gaseous nitrogen is transformed, or “fixed” into more readily available forms such as ammonia

Bis2A 09.0 Membranes: Components and Structure

By the end of this section, you will be able to:

- Understand the fluid mosaic model of cell membranes
- Describe the functions of phospholipids, proteins, and carbohydrates in membranes
- Discuss membrane fluidity

CELL MEMBRANES

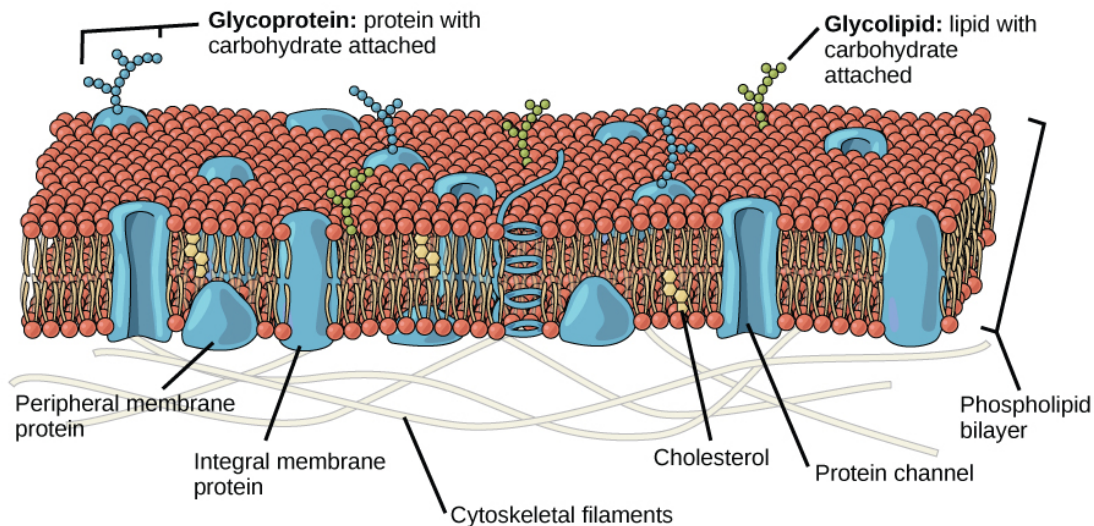
A cell's plasma membrane defines the cell, outlines its borders, and determines the nature of its interaction with its environment (see [\[link\]](#) for a summary). Cells exclude some substances, take in others, and excrete still others, all in controlled quantities. The plasma membrane must be very flexible to allow certain cells, such as red blood cells and white blood cells, to change shape as they pass through narrow capillaries. These are the more obvious functions of a plasma membrane. In addition, the surface of the plasma membrane carries markers that allow cells to recognize one another, which is vital for tissue and organ formation during early development, and which later plays a role in the “self” versus “non-self” distinction of the immune response. Insert paragraph text here.

Among the most sophisticated functions of the plasma membrane is the ability to transmit signals by means of complex, integral proteins known as receptors. These proteins act both as receivers of extracellular inputs and as activators of intracellular processes. These membrane receptors provide extracellular attachment sites for effectors like hormones and growth factors, and they activate intracellular response cascades when their effectors are bound. Occasionally, receptors are hijacked by viruses (HIV, human immunodeficiency virus, is one example) that use them to gain entry into cells, and at times, the genes encoding receptors become mutated, causing the process of signal transduction to malfunction with disastrous consequences.

Fluid Mosaic Model

The existence of the plasma membrane was identified in the 1890s, and its chemical components were identified in 1915. The principal components identified at that time were lipids and proteins. The first widely accepted model of the plasma membrane's structure was proposed in 1935 by Hugh Davson and James Danielli; it was based on the “railroad track” appearance of the plasma membrane in early electron micrographs. They theorized that the structure of the plasma membrane resembles a sandwich, with protein being analogous to the bread, and lipids being analogous to the filling. In the 1950s, advances in microscopy, notably transmission electron microscopy (TEM), allowed researchers to see that the core of the plasma membrane consisted of a double, rather than a single, layer. A new model that better explains both the microscopic observations and the function of that plasma membrane was proposed by S.J. Singer and Garth L. Nicolson in 1972.

The explanation proposed by Singer and Nicolson is called the **fluid mosaic model**. The model has evolved somewhat over time, but it still best accounts for the structure and functions of the plasma membrane as we now understand them. The fluid mosaic model describes the structure of the plasma membrane as a mosaic of components—including phospholipids, cholesterol, proteins, and carbohydrates—that gives the membrane a fluid character. Plasma membranes range from 5 to 10 nm in thickness. For comparison, human red blood cells, visible via light microscopy, are approximately 8 μm wide, or approximately 1,000 times wider than a plasma membrane. The membrane does look a bit like a sandwich ([\[link\]](#)).



The fluid mosaic model of the plasma membrane describes the plasma membrane as a fluid combination of phospholipids, cholesterol, and proteins. Carbohydrates attached to lipids (glycolipids) and to proteins (glycoproteins) extend from the outward-facing surface of the membrane.

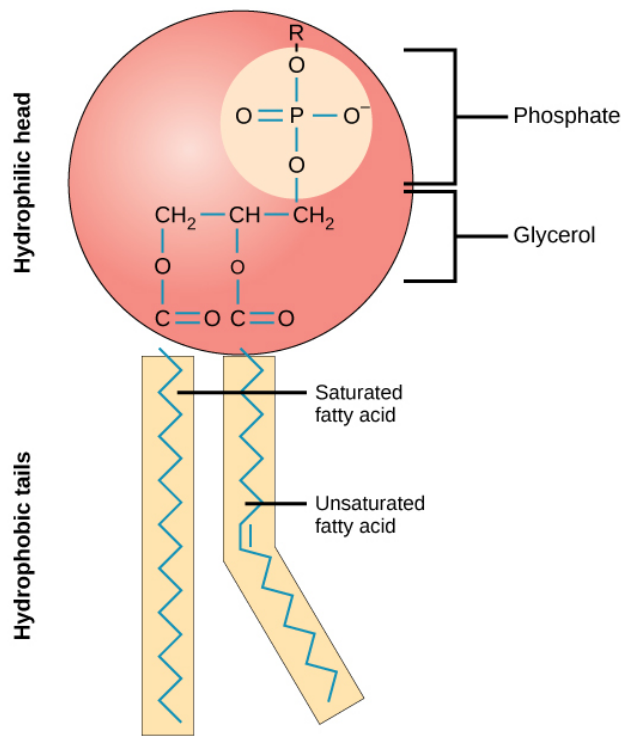
The principal components of a plasma membrane are lipids (phospholipids and cholesterol), proteins, and carbohydrates attached to some of the lipids and some of the proteins. A phospholipid is a molecule consisting of glycerol, two fatty acids, and a phosphate-linked head group. Cholesterol, another lipid composed of four fused carbon rings, is found alongside the phospholipids in the core of the membrane. The proportions of proteins, lipids, and carbohydrates in the plasma membrane vary with cell type, but for a typical human cell, protein accounts for about 50 percent of the composition by mass, lipids (of all types) account for about 40 percent of the composition by mass, with the remaining 10 percent of the composition by mass being carbohydrates. However, the concentration of proteins and lipids varies with different cell membranes. For example, myelin, an outgrowth of the membrane of specialized cells that insulates the axons of the peripheral nerves, contains only 18 percent protein and 76 percent lipid. The mitochondrial inner membrane contains 76 percent protein and only 24 percent lipid. The plasma membrane of human red blood cells is 30 percent

lipid. Carbohydrates are present only on the exterior surface of the plasma membrane and are attached to proteins, forming **glycoproteins**, or attached to lipids, forming **glycolipids**.

Phospholipids

The main fabric of the membrane is composed of amphiphilic, phospholipid molecules. The **hydrophilic** or “water-loving” areas of these molecules (which look like a collection of balls in an artist’s rendition of the model) ([\[link\]](#)) are in contact with the aqueous fluid both inside and outside the cell. **Hydrophobic**, or water-hating molecules, tend to be non-polar. They interact with other non-polar molecules in chemical reactions, but generally do not interact with polar molecules. When placed in water, hydrophobic molecules tend to form a ball or cluster. The hydrophilic regions of the phospholipids tend to form hydrogen bonds with water and other polar molecules on both the exterior and interior of the cell. Thus, the membrane surfaces that face the interior and exterior of the cell are hydrophilic. In contrast, the interior of the cell membrane is hydrophobic and will not interact with water. Therefore, phospholipids form an excellent two-layer cell membrane that separates fluid within the cell from the fluid outside of the cell.

A phospholipid molecule ([\[link\]](#)) consists of a three-carbon glycerol backbone with two fatty acid molecules attached to carbons 1 and 2, and a phosphate-containing group attached to the third carbon. This arrangement gives the overall molecule an area described as its head (the phosphate-containing group), which has a polar character or negative charge, and an area called the tail (the fatty acids), which has no charge. The head can form hydrogen bonds, but the tail cannot. A molecule with this arrangement of a positively or negatively charged area and an uncharged, or non-polar, area is referred to as **amphiphilic** or “dual-loving.”

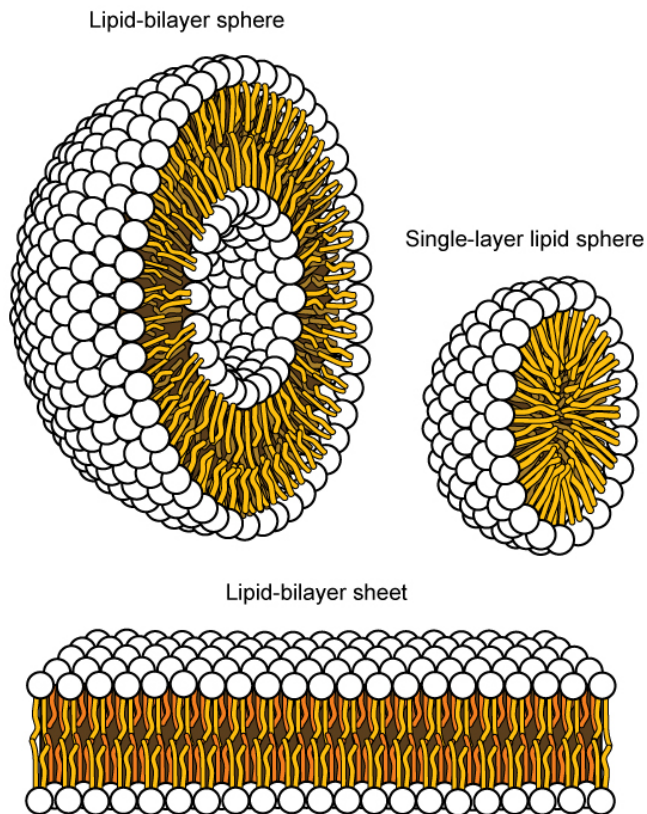


This phospholipid molecule is composed of a hydrophilic head and two hydrophobic tails. The hydrophilic head group consists of a phosphate-containing group attached to a glycerol molecule.

The hydrophobic tails, each containing either a saturated or an unsaturated fatty acid, are long hydrocarbon chains.

This characteristic is vital to the structure of a plasma membrane because, in water, phospholipids tend to become arranged with their hydrophobic tails facing each other and their hydrophilic heads facing out. In this way, they form a lipid bilayer—a barrier composed of a double layer of phospholipids that separates the water and other materials on one side of the barrier from the water and other materials on the other side. In fact, phospholipids heated in an aqueous solution tend to spontaneously form

small spheres or droplets (called micelles or liposomes), with their hydrophilic heads forming the exterior and their hydrophobic tails on the inside ([link](#)).

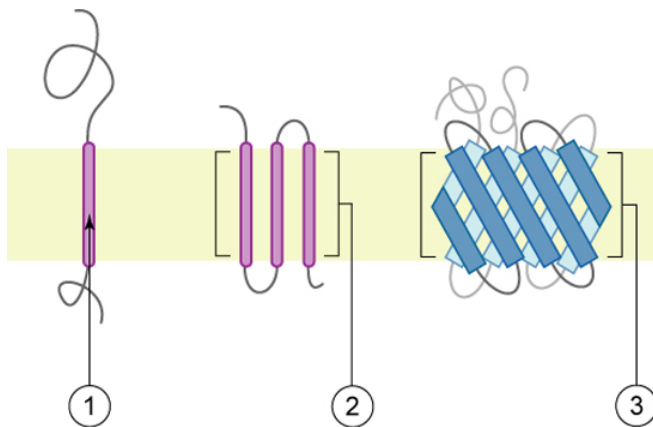


In an aqueous solution, phospholipids tend to arrange themselves with their polar heads facing outward and their hydrophobic tails facing inward.
(credit: modification of work by Mariana Ruiz Villareal)

Proteins

Proteins make up the second major component of plasma membranes.

Integral proteins (some specialized types are called integrins) are, as their name suggests, integrated completely into the membrane structure, and their hydrophobic membrane-spanning regions interact with the hydrophobic region of the phospholipid bilayer ([\[link\]](#)). Single-pass integral membrane proteins usually have a hydrophobic transmembrane segment that consists of 20–25 amino acids. Some span only part of the membrane—associating with a single layer—while others stretch from one side of the membrane to the other, and are exposed on either side. Some complex proteins are composed of up to 12 segments of a single protein, which are extensively folded and embedded in the membrane ([\[link\]](#)). This type of protein has a hydrophilic region or regions, and one or several mildly hydrophobic regions. This arrangement of regions of the protein tends to orient the protein alongside the phospholipids, with the hydrophobic region of the protein adjacent to the tails of the phospholipids and the hydrophilic region or regions of the protein protruding from the membrane and in contact with the cytosol or extracellular fluid.



Integral membranes proteins may have one or more alpha-helices that span the membrane (examples 1 and 2), or they may have beta-sheets that span the membrane (example 3). (credit: “Foobar”/Wikimedia Commons)

Peripheral proteins are found on the exterior and interior surfaces of membranes, attached either to integral proteins or to phospholipids. Peripheral proteins, along with integral proteins, may serve as enzymes, as structural attachments for the fibers of the cytoskeleton, or as part of the cell's recognition sites. These are sometimes referred to as “cell-specific” proteins. The body recognizes its own proteins and attacks foreign proteins associated with invasive pathogens.

Carbohydrates

Carbohydrates are the third major component of plasma membranes. They are always found on the exterior surface of cells and are bound either to proteins (forming glycoproteins) or to lipids (forming glycolipids) ([\[link\]](#)). These carbohydrate chains may consist of 2–60 monosaccharide units and can be either straight or branched. Along with peripheral proteins, carbohydrates form specialized sites on the cell surface that allow cells to recognize each other. These sites have unique patterns that allow the cell to be recognized, much the way that the facial features unique to each person allow him or her to be recognized. This recognition function is very important to cells, as it allows the immune system to differentiate between body cells (called “self”) and foreign cells or tissues (called “non-self”). Similar types of glycoproteins and glycolipids are found on the surfaces of viruses and may change frequently, preventing immune cells from recognizing and attacking them.

These carbohydrates on the exterior surface of the cell—the carbohydrate components of both glycoproteins and glycolipids—are collectively referred to as the glycocalyx (meaning “sugar coating”). The glycocalyx is highly hydrophilic and attracts large amounts of water to the surface of the cell. This aids in the interaction of the cell with its watery environment and in the cell's ability to obtain substances dissolved in the water. As discussed above, the glycocalyx is also important for cell identification, self/non-self

determination, and embryonic development, and is used in cell-cell attachments to form tissues.

Membrane Fluidity

The mosaic characteristic of the membrane, described in the fluid mosaic model, helps to illustrate its nature. The integral proteins and lipids exist in the membrane as separate but loosely attached molecules. These resemble the separate, multicolored tiles of a mosaic picture, and they float, moving somewhat with respect to one another. The membrane is not like a balloon, however, that can expand and contract; rather, it is fairly rigid and can burst if penetrated or if a cell takes in too much water. However, because of its mosaic nature, a very fine needle can easily penetrate a plasma membrane without causing it to burst, and the membrane will flow and self-seal when the needle is extracted.

The mosaic characteristics of the membrane explain some but not all of its fluidity. There are two other factors that help maintain this fluid characteristic. One factor is the nature of the phospholipids themselves. In their saturated form, the fatty acids in phospholipid tails are saturated with bound hydrogen atoms. There are no double bonds between adjacent carbon atoms. This results in tails that are relatively straight. In contrast, unsaturated fatty acids do not contain a maximal number of hydrogen atoms, but they do contain some double bonds between adjacent carbon atoms; a double bond results in a bend in the string of carbons of approximately 30 degrees ([\[link\]](#)).

Thus, if saturated fatty acids, with their straight tails, are compressed by decreasing temperatures, they press in on each other, making a dense and fairly rigid membrane. If unsaturated fatty acids are compressed, the “kinks” in their tails elbow adjacent phospholipid molecules away, maintaining some space between the phospholipid molecules. This “elbow room” helps to maintain fluidity in the membrane at temperatures at which membranes with saturated fatty acid tails in their phospholipids would “freeze” or solidify. The relative fluidity of the membrane is particularly important in a cold environment. A cold environment tends to compress membranes composed largely of saturated fatty acids, making them less

fluid and more susceptible to rupturing. Many organisms (fish are one example) are capable of adapting to cold environments by changing the proportion of unsaturated fatty acids in their membranes in response to the lowering of the temperature.

Note:

Link to Learning



Visit this [site](#) to see animations of the fluidity and mosaic quality of membranes.

Animals have an additional membrane constituent that assists in maintaining fluidity. Cholesterol, which lies alongside the phospholipids in the membrane, tends to dampen the effects of temperature on the membrane. Thus, this lipid functions as a buffer, preventing lower temperatures from inhibiting fluidity and preventing increased temperatures from increasing fluidity too much. Thus, cholesterol extends, in both directions, the range of temperature in which the membrane is appropriately fluid and consequently functional. Cholesterol also serves other functions, such as organizing clusters of transmembrane proteins into lipid rafts.

The Components and Functions of the Plasma Membrane

The Components and Functions of the Plasma Membrane	
Component	Location
Phospholipid	Main fabric of the membrane
Cholesterol	Attached between phospholipids and between the two phospholipid layers
Integral proteins (for example, integrins)	Embedded within the phospholipid layer(s). May or may not penetrate through both layers
Peripheral proteins	On the inner or outer surface of the phospholipid bilayer; not embedded within the phospholipids
Carbohydrates (components of glycoproteins and glycolipids)	Generally attached to proteins on the outside membrane layer

Section Summary

The modern understanding of the plasma membrane is referred to as the fluid mosaic model. The plasma membrane is composed of a bilayer of phospholipids, with their hydrophobic, fatty acid tails in contact with each other. The landscape of the membrane is studded with proteins, some of which span the membrane. Some of these proteins serve to transport materials into or out of the cell. Carbohydrates are attached to some of the proteins and lipids on the outward-facing surface of the membrane, forming complexes that function to identify the cell to other cells. The fluid nature of the membrane is due to temperature, the configuration of the fatty acid tails (some kinked by double bonds), the presence of cholesterol embedded in the membrane, and the mosaic nature of the proteins and protein-

carbohydrate combinations, which are not firmly fixed in place. Plasma membranes enclose and define the borders of cells, but rather than being a static bag, they are dynamic and constantly in flux.

Review Questions

Exercise:

Problem:

Which plasma membrane component can be either found on its surface or embedded in the membrane structure?

- a. protein
- b. cholesterol
- c. carbohydrate
- d. phospholipid

Solution:

A

Exercise:

Problem:

Which characteristic of a phospholipid contributes to the fluidity of the membrane?

- a. its head
- b. cholesterol
- c. a saturated fatty acid tail
- d. double bonds in the fatty acid tail

Solution:

D

Exercise:**Problem:**

What is the primary function of carbohydrates attached to the exterior of cell membranes?

- a. identification of the cell
- b. flexibility of the membrane
- c. strengthening the membrane
- d. channels through membrane

Solution:

A

Free Response**Exercise:****Problem:**

Why is it advantageous for the cell membrane to be fluid in nature?

Solution:

The fluid characteristic of the cell membrane allows greater flexibility to the cell than it would if the membrane were rigid. It also allows the motion of membrane components, required for some types of membrane transport.

Exercise:**Problem:**

Why do phospholipids tend to spontaneously orient themselves into something resembling a membrane?

Solution:

The hydrophobic, nonpolar regions must align with each other in order for the structure to have minimal potential energy and, consequently, higher stability. The fatty acid tails of the phospholipids cannot mix with water, but the phosphate “head” of the molecule can. Thus, the head orients to water, and the tail to other lipids.

Glossary

amphiphilic

molecule possessing a polar or charged area and a nonpolar or uncharged area capable of interacting with both hydrophilic and hydrophobic environments

fluid mosaic model

describes the structure of the plasma membrane as a mosaic of components including phospholipids, cholesterol, proteins, glycoproteins, and glycolipids (sugar chains attached to proteins or lipids, respectively), resulting in a fluid character (fluidity)

glycolipid

combination of carbohydrates and lipids

glycoprotein

combination of carbohydrates and proteins

hydrophilic

molecule with the ability to bond with water; “water-loving”

hydrophobic

molecule that does not have the ability to bond with water; “water-hating”

integral protein

protein integrated into the membrane structure that interacts extensively with the hydrocarbon chains of membrane lipids and often

spans the membrane; these proteins can be removed only by the disruption of the membrane by detergents

peripheral protein

protein found at the surface of a plasma membrane either on its exterior or interior side; these proteins can be removed (washed off of the membrane) by a high-salt wash

Bis2A 09.1 Passive Transport

By the end of this section, you will be able to:

- Explain why and how passive transport occurs
- Understand the processes of osmosis and diffusion
- Define tonicity and describe its relevance to passive transport

Transport across the membrane

One of the great wonders of the cell membrane is its ability to regulate the concentration of substances inside the cell. These substances include ions such as Ca^{++} , Na^+ , K^+ , and Cl^- ; nutrients including sugars, fatty acids, and amino acids; and waste products, particularly carbon dioxide (CO_2), which must leave the cell.

The membrane's lipid bilayer structure provides the first level of control. The phospholipids are tightly packed together, and the membrane has a hydrophobic interior. This structure causes the membrane to be selectively permeable. A membrane that has **selective permeability** allows only substances meeting certain criteria to pass through it unaided. In the case of the cell membrane, only relatively small, nonpolar materials can move through the lipid bilayer (remember, the lipid tails of the membrane are nonpolar). Some examples of these are other lipids, oxygen and carbon dioxide gases, and alcohol. However, water-soluble materials—like glucose, amino acids, and electrolytes—need some assistance to cross the membrane because they are repelled by the hydrophobic tails of the phospholipid bilayer. All substances that move through the membrane do so by one of two general methods, which are categorized based on whether or not energy is required. **Passive transport** is the movement of substances across the membrane without the expenditure of cellular energy. In contrast, **active transport** is the movement of substances across the membrane using energy from adenosine triphosphate (ATP).

Passive Transport

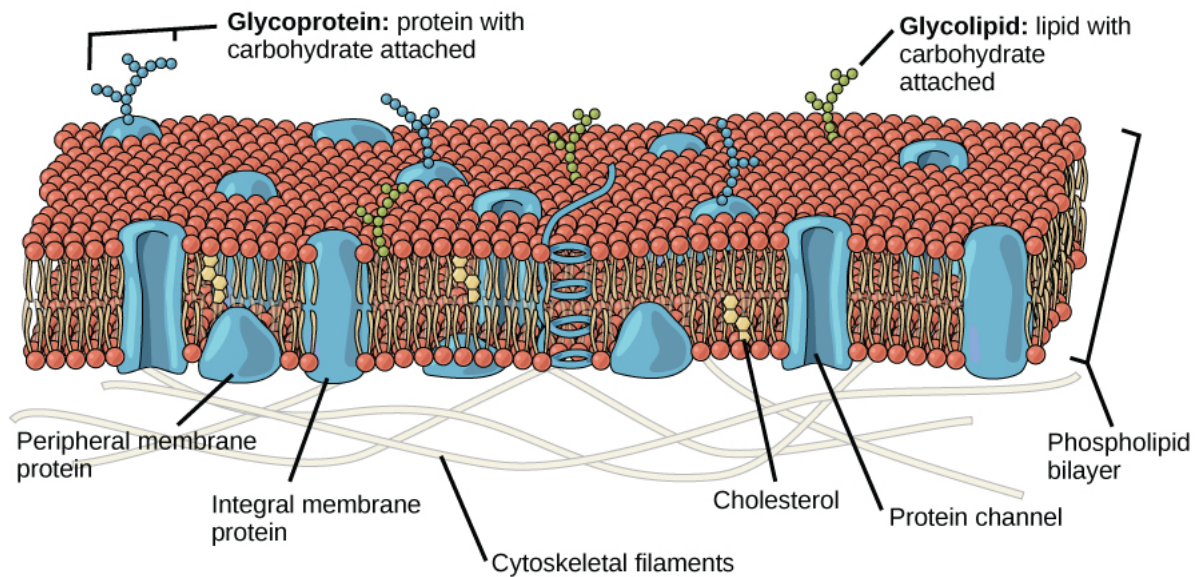
Plasma membranes must allow certain substances to enter and leave a cell, and prevent some harmful materials from entering and some essential

materials from leaving. In other words, plasma membranes are **selectively permeable**—they allow some substances to pass through, but not others. If they were to lose this selectivity, the cell would no longer be able to sustain itself, and it would be destroyed. Some cells require larger amounts of specific substances than do other cells; they must have a way of obtaining these materials from extracellular fluids. This may happen passively, as certain materials move back and forth, or the cell may have special mechanisms that facilitate transport. Some materials are so important to a cell that it spends some of its energy, hydrolyzing adenosine triphosphate (ATP), to obtain these materials. Red blood cells use some of their energy doing just that. All cells spend the majority of their energy to maintain an imbalance of sodium and potassium ions between the interior and exterior of the cell.

The most direct forms of membrane transport are passive. **Passive transport** is a naturally occurring phenomenon and does not require the cell to exert any of its energy to accomplish the movement. In passive transport, substances move from an area of higher concentration to an area of lower concentration. A physical space in which there is a range of concentrations of a single substance is said to have a **concentration gradient**.

Selective Permeability

Plasma membranes are asymmetric: the interior of the membrane is not identical to the exterior of the membrane. In fact, there is a considerable difference between the array of phospholipids and proteins between the two leaflets that form a membrane. On the interior of the membrane, some proteins serve to anchor the membrane to fibers of the cytoskeleton. There are peripheral proteins on the exterior of the membrane that bind elements of the extracellular matrix. Carbohydrates, attached to lipids or proteins, are also found on the exterior surface of the plasma membrane. These carbohydrate complexes help the cell bind substances that the cell needs in the extracellular fluid. This adds considerably to the selective nature of plasma membranes ([link](#)).



The exterior surface of the plasma membrane is not identical to the interior surface of the same membrane.

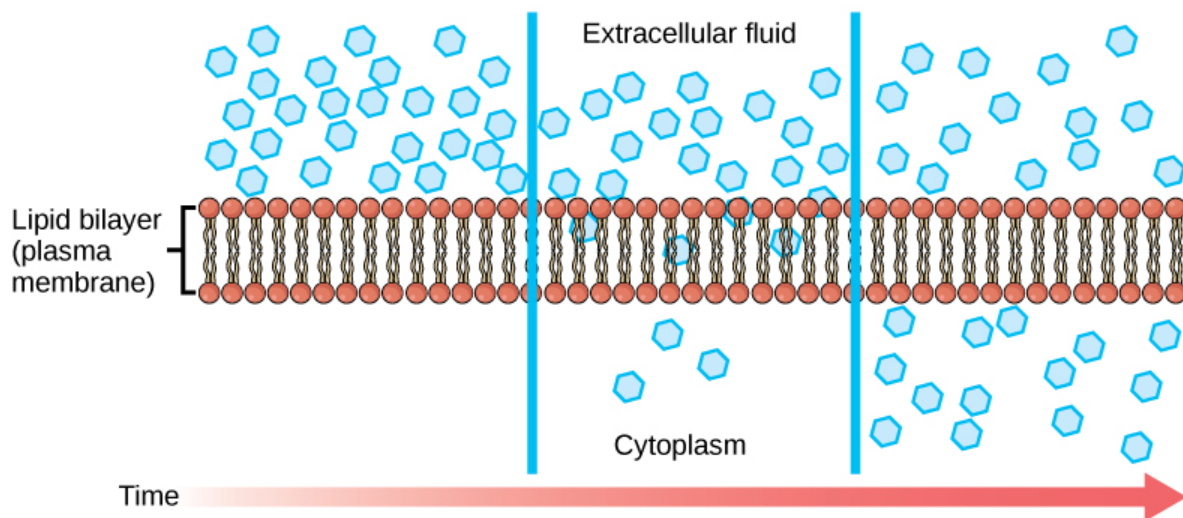
Recall that plasma membranes are amphiphilic: They have hydrophilic and hydrophobic regions. This characteristic helps the movement of some materials through the membrane and hinders the movement of others. Lipid-soluble material with a low molecular weight can easily slip through the hydrophobic lipid core of the membrane. Substances such as the fat-soluble vitamins A, D, E, and K readily pass through the plasma membranes in the digestive tract and other tissues. Fat-soluble drugs and hormones also gain easy entry into cells and are readily transported into the body's tissues and organs. Molecules of oxygen and carbon dioxide have no charge and so pass through membranes by simple diffusion.

Polar substances present problems for the membrane. While some polar molecules connect easily with the outside of a cell, they cannot readily pass through the lipid core of the plasma membrane. Additionally, while small ions could easily slip through the spaces in the mosaic of the membrane, their charge prevents them from doing so. Ions such as sodium, potassium, calcium, and chloride must have special means of penetrating plasma membranes. Simple sugars and amino acids also need help with transport

across plasma membranes, achieved by various transmembrane proteins (channels).

Diffusion

Diffusion is a passive process of transport. A single substance tends to move from an area of high concentration to an area of low concentration until the concentration is equal across a space. You are familiar with diffusion of substances through the air. For example, think about someone opening a bottle of ammonia in a room filled with people. The ammonia gas is at its highest concentration in the bottle; its lowest concentration is at the edges of the room. The ammonia vapor will diffuse, or spread away, from the bottle, and gradually, more and more people will smell the ammonia as it spreads. Materials move within the cell's cytosol by diffusion, and certain materials move through the plasma membrane by diffusion ([\[link\]](#)). Diffusion expends no energy. On the contrary, concentration gradients are a form of potential energy, dissipated as the gradient is eliminated.



Diffusion through a permeable membrane moves a substance from an area of high concentration (extracellular fluid, in this case) down its concentration gradient (into the cytoplasm). (credit: modification of work by Mariana Ruiz Villareal)

Each separate substance in a medium, such as the extracellular fluid, has its own concentration gradient, independent of the concentration gradients of other materials. In addition, each substance will diffuse according to that gradient. Within a system, there will be different rates of diffusion of the different substances in the medium.

Factors That Affect Diffusion

Molecules move constantly in a random manner, at a rate that depends on their mass, their environment, and the amount of thermal energy they possess, which in turn is a function of temperature. This movement accounts for the diffusion of molecules through whatever medium in which they are localized. A substance will tend to move into any space available to it until it is evenly distributed throughout it. After a substance has diffused completely through a space, removing its concentration gradient, molecules will still move around in the space, but there will be no *net* movement of the number of molecules from one area to another. This lack of a concentration gradient in which there is no net movement of a substance is known as dynamic equilibrium. While diffusion will go forward in the presence of a concentration gradient of a substance, several factors affect the rate of diffusion.

- **Extent of the concentration gradient:** The greater the difference in concentration, the more rapid the diffusion. The closer the distribution of the material gets to equilibrium, the slower the rate of diffusion becomes.
- **Mass of the molecules diffusing:** Heavier molecules move more slowly; therefore, they diffuse more slowly. The reverse is true for lighter molecules.
- **Temperature:** Higher temperatures increase the energy and therefore the movement of the molecules, increasing the rate of diffusion. Lower temperatures decrease the energy of the molecules, thus decreasing the rate of diffusion.

- **Solvent density:** As the density of a solvent increases, the rate of diffusion decreases. The molecules slow down because they have a more difficult time getting through the denser medium. If the medium is less dense, diffusion increases. Because cells primarily use diffusion to move materials within the cytoplasm, any increase in the cytoplasm's density will inhibit the movement of the materials. An example of this is a person experiencing dehydration. As the body's cells lose water, the rate of diffusion decreases in the cytoplasm, and the cells' functions deteriorate. Neurons tend to be very sensitive to this effect. Dehydration frequently leads to unconsciousness and possibly coma because of the decrease in diffusion rate within the cells.
- **Solubility:** As discussed earlier, nonpolar or lipid-soluble materials pass through plasma membranes more easily than polar materials, allowing a faster rate of diffusion.
- **Surface area and thickness of the plasma membrane:** Increased surface area increases the rate of diffusion, whereas a thicker membrane reduces it.
- **Distance travelled:** The greater the distance that a substance must travel, the slower the rate of diffusion. This places an upper limitation on cell size. A large, spherical cell will die because nutrients or waste cannot reach or leave the center of the cell, respectively. Therefore, cells must either be small in size, as in the case of many prokaryotes, or be flattened, as with many single-celled eukaryotes.

A variation of diffusion is the process of filtration. In filtration, material moves according to its concentration gradient through a membrane; sometimes the rate of diffusion is enhanced by pressure, causing the substances to filter more rapidly. This occurs in the kidney, where blood pressure forces large amounts of water and accompanying dissolved substances, or **solutes**, out of the blood and into the renal tubules. The rate of diffusion in this instance is almost totally dependent on pressure. One of the effects of high blood pressure is the appearance of protein in the urine, which is “squeezed through” by the abnormally high pressure.

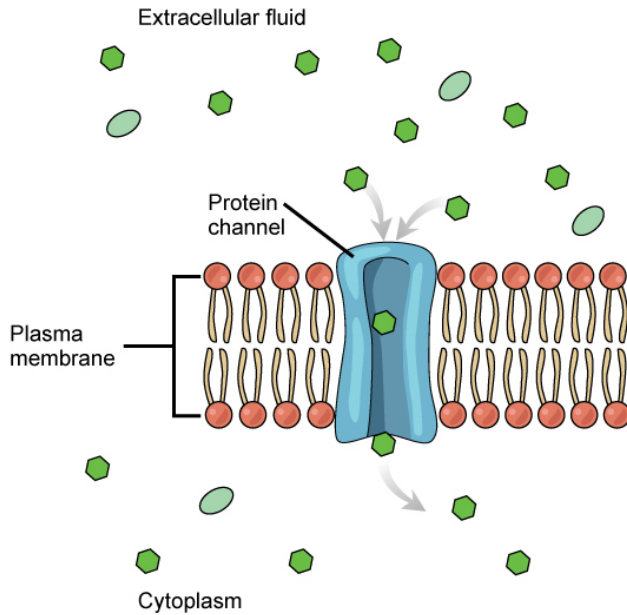
Facilitated transport

In **facilitated transport**, also called facilitated diffusion, materials diffuse across the plasma membrane with the help of membrane proteins. A concentration gradient exists that would allow these materials to diffuse into the cell without expending cellular energy. However, these materials are ions or polar molecules that are repelled by the hydrophobic parts of the cell membrane. Facilitated transport proteins shield these materials from the repulsive force of the membrane, allowing them to diffuse into the cell.

The material being transported is first attached to protein or glycoprotein receptors on the exterior surface of the plasma membrane. This allows the material that is needed by the cell to be removed from the extracellular fluid. The substances are then passed to specific integral proteins that facilitate their passage. Some of these integral proteins are collections of beta pleated sheets that form a pore or channel through the phospholipid bilayer. Others are carrier proteins which bind with the substance and aid its diffusion through the membrane.

Channels

The integral proteins involved in facilitated transport are collectively referred to as **transport proteins**, and they function as either channels for the material or carriers. In both cases, they are transmembrane proteins. Channels are specific for the substance that is being transported. **Channel proteins** have hydrophilic domains exposed to the intracellular and extracellular fluids; they additionally have a hydrophilic channel through their core that provides a hydrated opening through the membrane layers ([link](#)). Passage through the channel allows polar compounds to avoid the nonpolar central layer of the plasma membrane that would otherwise slow or prevent their entry into the cell. **Aquaporins** are channel proteins that allow water to pass through the membrane at a very high rate.



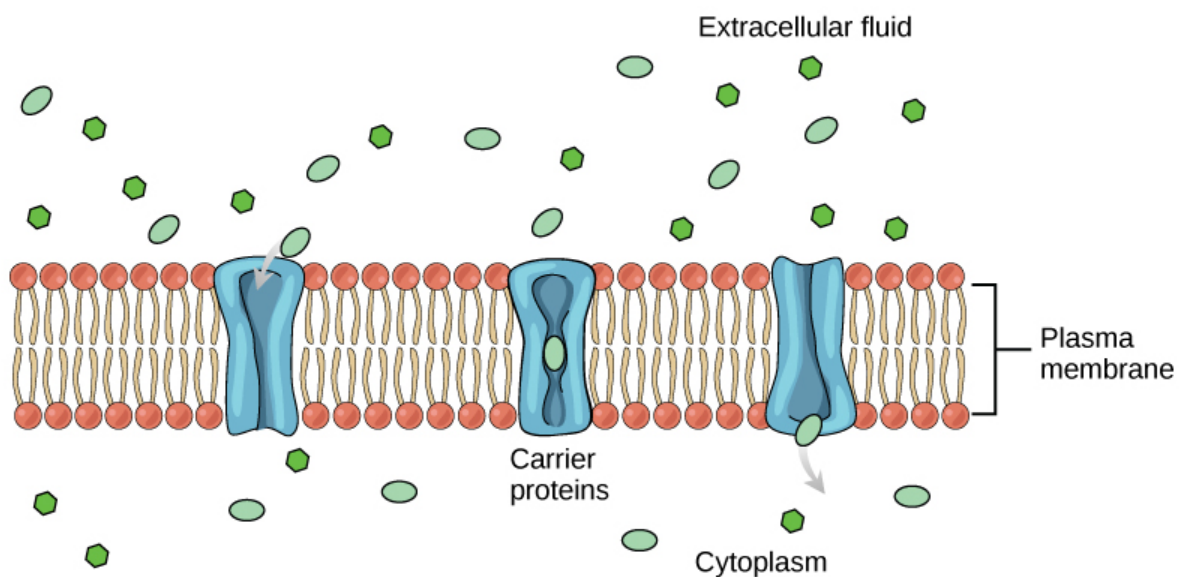
Facilitated transport moves substances down their concentration gradients. They may cross the plasma membrane with the aid of channel proteins. (credit: modification of work by Mariana Ruiz Villareal)

Channel proteins are either open at all times or they are “gated,” which controls the opening of the channel. The attachment of a particular ion to the channel protein may control the opening, or other mechanisms or substances may be involved. In some tissues, sodium and chloride ions pass freely through open channels, whereas in other tissues a gate must be opened to allow passage. An example of this occurs in the kidney, where both forms of channels are found in different parts of the renal tubules. Cells involved in the transmission of electrical impulses, such as nerve and muscle cells, have gated channels for sodium, potassium, and calcium in their membranes. Opening and closing of these channels changes the relative concentrations on opposing sides of the membrane of these ions, resulting in the facilitation of electrical transmission along membranes (in

the case of nerve cells) or in muscle contraction (in the case of muscle cells).

Carrier Proteins

Another type of protein embedded in the plasma membrane is a **carrier protein**. This aptly named protein binds a substance and, in doing so, triggers a change of its own shape, moving the bound molecule from the outside of the cell to its interior ([link](#)); depending on the gradient, the material may move in the opposite direction. Carrier proteins are typically specific for a single substance. This selectivity adds to the overall selectivity of the plasma membrane. The exact mechanism for the change of shape is poorly understood. Proteins can change shape when their hydrogen bonds are affected, but this may not fully explain this mechanism. Each carrier protein is specific to one substance, and there are a finite number of these proteins in any membrane. This can cause problems in transporting enough of the material for the cell to function properly. When all of the proteins are bound to their ligands, they are saturated and the rate of transport is at its maximum. Increasing the concentration gradient at this point will not result in an increased rate of transport.



Some substances are able to move down their concentration gradient across the plasma membrane with the aid of carrier proteins. Carrier proteins change shape as they move molecules across the membrane.
(credit: modification of work by Mariana Ruiz Villareal)

An example of this process occurs in the kidney. Glucose, water, salts, ions, and amino acids needed by the body are filtered in one part of the kidney. This filtrate, which includes glucose, is then reabsorbed in another part of the kidney. Because there are only a finite number of carrier proteins for glucose, if more glucose is present than the proteins can handle, the excess is not transported and it is excreted from the body in the urine. In a diabetic individual, this is described as “spilling glucose into the urine.” A different group of carrier proteins called glucose transport proteins, or GLUTs, are involved in transporting glucose and other hexose sugars through plasma membranes within the body.

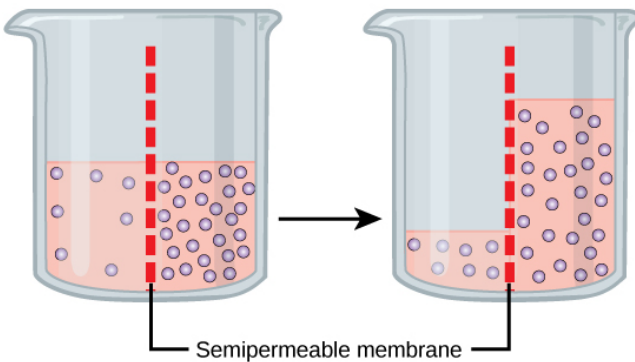
Channel and carrier proteins transport material at different rates. Channel proteins transport much more quickly than do carrier proteins. Channel proteins facilitate diffusion at a rate of tens of millions of molecules per second, whereas carrier proteins work at a rate of a thousand to a million molecules per second.

Osmosis

Osmosis is the movement of water through a semipermeable membrane according to the concentration gradient of water across the membrane, which is inversely proportional to the concentration of solutes. While diffusion transports material across membranes and within cells, osmosis transports *only water* across a membrane and the membrane limits the diffusion of solutes in the water. Not surprisingly, the aquaporins that facilitate water movement play a large role in osmosis, most prominently in red blood cells and the membranes of kidney tubules.

Mechanism

Osmosis is a special case of diffusion. Water, like other substances, moves from an area of high concentration to one of low concentration. An obvious question is what makes water move at all? Imagine a beaker with a semipermeable membrane separating the two sides or halves ([\[link\]](#)). On both sides of the membrane the water level is the same, but there are different concentrations of a dissolved substance, or **solute**, that cannot cross the membrane (otherwise the concentrations on each side would be balanced by the solute crossing the membrane). If the volume of the solution on both sides of the membrane is the same, but the concentrations of solute are different, then there are different amounts of water, the solvent, on either side of the membrane.



In osmosis, water always moves from an area of higher water concentration to one of lower concentration. In the diagram shown, the solute cannot pass through the selectively permeable membrane, but the water can.

To illustrate this, imagine two full glasses of water. One has a single teaspoon of sugar in it, whereas the second one contains one-quarter cup of sugar. If the total volume of the solutions in both cups is the same, which

cup contains more water? Because the large amount of sugar in the second cup takes up much more space than the teaspoon of sugar in the first cup, the first cup has more water in it.

Returning to the beaker example, recall that it has a mixture of solutes on either side of the membrane. A principle of diffusion is that the molecules move around and will spread evenly throughout the medium if they can. However, only the material capable of getting through the membrane will diffuse through it. In this example, the solute cannot diffuse through the membrane, but the water can. Water has a concentration gradient in this system. Thus, water will diffuse down its concentration gradient, crossing the membrane to the side where it is less concentrated. This diffusion of water through the membrane—osmosis—will continue until the concentration gradient of water goes to zero or until the hydrostatic pressure of the water balances the osmotic pressure. Osmosis proceeds constantly in living systems.

Tonicity

Tonicity describes how an extracellular solution can change the volume of a cell by affecting osmosis. A solution's tonicity often directly correlates with the osmolarity of the solution. **Osmolarity** describes the total solute concentration of the solution. A solution with low osmolarity has a greater number of water molecules relative to the number of solute particles; a solution with high osmolarity has fewer water molecules with respect to solute particles. In a situation in which solutions of two different osmolarities are separated by a membrane permeable to water, though not to the solute, water will move from the side of the membrane with lower osmolarity (and more water) to the side with higher osmolarity (and less water). This effect makes sense if you remember that the solute cannot move across the membrane, and thus the only component in the system that can move—the water—moves along its own concentration gradient. An important distinction that concerns living systems is that osmolarity measures the number of particles (which may be molecules) in a solution. Therefore, a solution that is cloudy with cells may have a lower osmolarity than a solution that is clear, if the second solution contains more dissolved molecules than there are cells.

Hypotonic Solutions

Three terms—hypotonic, isotonic, and hypertonic—are used to relate the osmolarity of a cell to the osmolarity of the extracellular fluid that contains the cells. In a **hypotonic** situation, the extracellular fluid has lower osmolarity than the fluid inside the cell, and water enters the cell. (In living systems, the point of reference is always the cytoplasm, so the prefix *hypo-* means that the extracellular fluid has a lower concentration of solutes, or a lower osmolarity, than the cell cytoplasm.) It also means that the extracellular fluid has a higher concentration of water in the solution than does the cell. In this situation, water will follow its concentration gradient and enter the cell.

Hypertonic Solutions

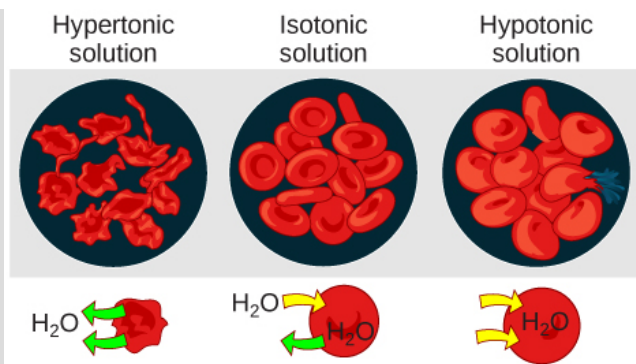
As for a **hypertonic** solution, the prefix *hyper-* refers to the extracellular fluid having a higher osmolarity than the cell's cytoplasm; therefore, the fluid contains less water than the cell does. Because the cell has a relatively higher concentration of water, water will leave the cell.

Isotonic Solutions

In an **isotonic** solution, the extracellular fluid has the same osmolarity as the cell. If the osmolarity of the cell matches that of the extracellular fluid, there will be no net movement of water into or out of the cell, although water will still move in and out. Blood cells and plant cells in hypertonic, isotonic, and hypotonic solutions take on characteristic appearances ([\[link\]](#)).

Note:

Art Connection



Osmotic pressure changes the shape of red blood cells in hypertonic, isotonic, and hypotonic solutions. (credit: Mariana Ruiz Villareal)

A doctor injects a patient with what the doctor thinks is an isotonic saline solution. The patient dies, and an autopsy reveals that many red blood cells have been destroyed. Do you think the solution the doctor injected was really isotonic?

Note:

Link to Learning



For a video illustrating the process of diffusion in solutions, visit this [site](#).

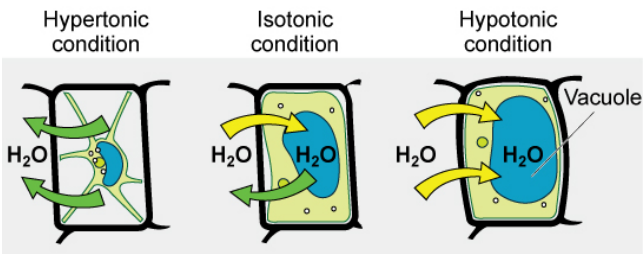
Tonicity in Living Systems

In a hypotonic environment, water enters a cell, and the cell swells. In an isotonic condition, the relative concentrations of solute and solvent are equal on both sides of the membrane. There is no net water movement; therefore, there is no change in the size of the cell. In a hypertonic solution, water leaves a cell and the cell shrinks. If either the hypo- or hyper-condition goes to excess, the cell's functions become compromised, and the cell may be destroyed.

A red blood cell will burst, or lyse, when it swells beyond the plasma membrane's capability to expand. Remember, the membrane resembles a mosaic, with discrete spaces between the molecules composing it. If the cell swells, and the spaces between the lipids and proteins become too large, the cell will break apart.

In contrast, when excessive amounts of water leave a red blood cell, the cell shrinks, or crenates. This has the effect of concentrating the solutes left in the cell, making the cytosol denser and interfering with diffusion within the cell. The cell's ability to function will be compromised and may also result in the death of the cell.

Various living things have ways of controlling the effects of osmosis—a mechanism called osmoregulation. Some organisms, such as plants, fungi, bacteria, and some protists, have cell walls that surround the plasma membrane and prevent cell lysis in a hypotonic solution. The plasma membrane can only expand to the limit of the cell wall, so the cell will not lyse. In fact, the cytoplasm in plants is always slightly hypertonic to the cellular environment, and water will always enter a cell if water is available. This inflow of water produces turgor pressure, which stiffens the cell walls of the plant ([\[link\]](#)). In nonwoody plants, turgor pressure supports the plant. Conversely, if the plant is not watered, the extracellular fluid will become hypertonic, causing water to leave the cell. In this condition, the cell does not shrink because the cell wall is not flexible. However, the cell membrane detaches from the wall and constricts the cytoplasm. This is called **plasmolysis**. Plants lose turgor pressure in this condition and wilt ([\[link\]](#)).



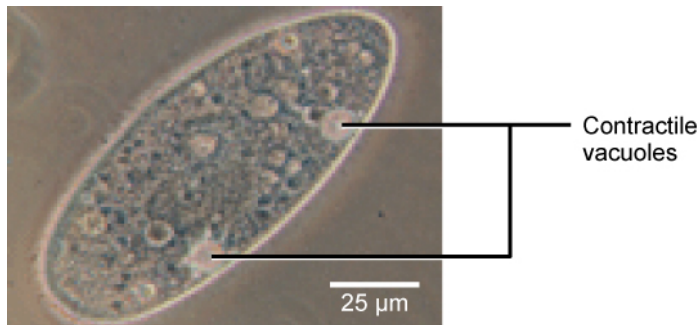
The turgor pressure within a plant cell depends on the tonicity of the solution that it is bathed in.
 (credit: modification of work by Mariana Ruiz Villareal)



Without adequate water, the plant on the left has lost turgor pressure, visible in its wilting; the turgor pressure is restored by watering it (right). (credit: Victor M. Vicente Selvas)

Tonicity is a concern for all living things. For example, paramecia and amoebas, which are protists that lack cell walls, have contractile vacuoles.

This vesicle collects excess water from the cell and pumps it out, keeping the cell from lysing as it takes on water from its environment ([\[link\]](#)).



A paramecium's contractile vacuole, here visualized using bright field light microscopy at 480x magnification, continuously pumps water out of the organism's body to keep it from bursting in a hypotonic medium. (credit: modification of work by NIH; scale-bar data from Matt Russell)

Many marine invertebrates have internal salt levels matched to their environments, making them isotonic with the water in which they live. Fish, however, must spend approximately five percent of their metabolic energy maintaining osmotic homeostasis. Freshwater fish live in an environment that is hypotonic to their cells. These fish actively take in salt through their gills and excrete diluted urine to rid themselves of excess water. Saltwater fish live in the reverse environment, which is hypertonic to their cells, and they secrete salt through their gills and excrete highly concentrated urine.

In vertebrates, the kidneys regulate the amount of water in the body. Osmoreceptors are specialized cells in the brain that monitor the concentration of solutes in the blood. If the levels of solutes increase beyond a certain range, a hormone is released that retards water loss

through the kidney and dilutes the blood to safer levels. Animals also have high concentrations of albumin, which is produced by the liver, in their blood. This protein is too large to pass easily through plasma membranes and is a major factor in controlling the osmotic pressures applied to tissues.

Section Summary

The passive forms of transport, diffusion and osmosis, move materials of small molecular weight across membranes. Substances diffuse from areas of high concentration to areas of lower concentration, and this process continues until the substance is evenly distributed in a system. In solutions containing more than one substance, each type of molecule diffuses according to its own concentration gradient, independent of the diffusion of other substances. Many factors can affect the rate of diffusion, including concentration gradient, size of the particles that are diffusing, temperature of the system, and so on.

In living systems, diffusion of substances into and out of cells is mediated by the plasma membrane. Some materials diffuse readily through the membrane, but others are hindered, and their passage is made possible by specialized proteins, such as channels and transporters. The chemistry of living things occurs in aqueous solutions, and balancing the concentrations of those solutions is an ongoing problem. In living systems, diffusion of some substances would be slow or difficult without membrane proteins that facilitate transport.

Art Connections

Exercise:

Problem:

[\[link\]](#) A doctor injects a patient with what the doctor thinks is an isotonic saline solution. The patient dies, and an autopsy reveals that many red blood cells have been destroyed. Do you think the solution the doctor injected was really isotonic?

Solution:

[\[link\]](#) No, it must have been hypotonic as a hypotonic solution would cause water to enter the cells, thereby making them burst.

Review Questions**Exercise:**

Problem: Water moves via osmosis _____.

- a. throughout the cytoplasm
- b. from an area with a high concentration of other solutes to a lower one
- c. from an area with a high concentration of water to one of lower concentration
- d. from an area with a low concentration of water to one of higher concentration

Solution:

C

Exercise:**Problem:**

The principal force driving movement in diffusion is the _____.

- a. temperature
- b. particle size
- c. concentration gradient
- d. membrane surface area

Solution:

C

Exercise:

Problem:What problem is faced by organisms that live in fresh water?

- a. Their bodies tend to take in too much water.
 - b. They have no way of controlling their tonicity.
 - c. Only salt water poses problems for animals that live in it.
 - d. Their bodies tend to lose too much water to their environment.
-

Solution:

A

Free Response

Exercise:

Problem:

Discuss why the following affect the rate of diffusion: molecular size, temperature, solution density, and the distance that must be traveled.

Solution:

Heavy molecules move more slowly than lighter ones. It takes more energy in the medium to move them along. Increasing or decreasing temperature increases or decreases the energy in the medium, affecting molecular movement. The denser a solution is, the harder it is for molecules to move through it, causing diffusion to slow down due to friction. Living cells require a steady supply of nutrients and a steady rate of waste removal. If the distance these substances need to travel is too great, diffusion cannot move nutrients and waste materials efficiently to sustain life.

Exercise:

Problem: Why does water move through a membrane?

Solution:

Water moves through a membrane in osmosis because there is a concentration gradient across the membrane of solute and solvent. The solute cannot effectively move to balance the concentration on both sides of the membrane, so water moves to achieve this balance.

Exercise:

Problem:

Both of the regular intravenous solutions administered in medicine, normal saline and lactated Ringer's solution, are isotonic. Why is this important?

Solution:

Injection of isotonic solutions ensures that there will be no perturbation of the osmotic balance, and no water taken from tissues or added to them from the blood.

Glossary

aquaporin

channel protein that allows water through the membrane at a very high rate

carrier protein

membrane protein that moves a substance across the plasma membrane by changing its own shape

channel protein

membrane protein that allows a substance to pass through its hollow core across the plasma membrane

concentration gradient

area of high concentration adjacent to an area of low concentration

diffusion

passive process of transport of low-molecular weight material according to its concentration gradient

facilitated transport

process by which material moves down a concentration gradient (from high to low concentration) using integral membrane proteins

hypertonic

situation in which extracellular fluid has a higher osmolarity than the fluid inside the cell, resulting in water moving out of the cell

hypotonic

situation in which extracellular fluid has a lower osmolarity than the fluid inside the cell, resulting in water moving into the cell

isotonic

situation in which the extracellular fluid has the same osmolarity as the fluid inside the cell, resulting in no net movement of water into or out of the cell

osmolarity

total amount of substances dissolved in a specific amount of solution

osmosis

transport of water through a semipermeable membrane according to the concentration gradient of water across the membrane that results from the presence of solute that cannot pass through the membrane

passive transport

method of transporting material through a membrane that does not require energy

plasmolysis

detaching of the cell membrane from the cell wall and constriction of the cell membrane when a plant cell is in a hypertonic solution

selectively permeable

characteristic of a membrane that allows some substances through but not others

solute

substance dissolved in a liquid to form a solution

tonicity

amount of solute in a solution

transport protein

membrane protein that facilitates passage of a substance across a membrane by binding it

Bis2A 09.2 Active Transport

By the end of this section, you will be able to:

- Understand how electrochemical gradients affect ions
- Distinguish between primary active transport and secondary active transport

ACTIVE TRANSPORT

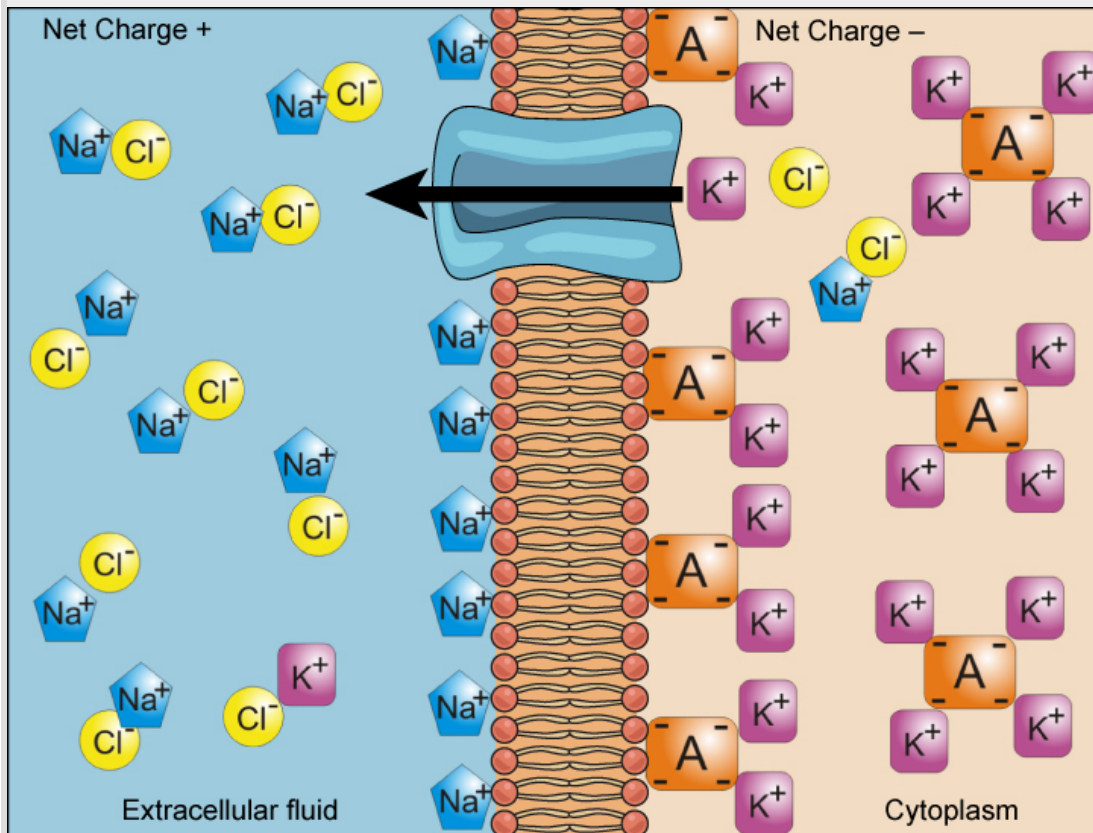
Active transport mechanisms require the use of the cell's energy, usually in the form of adenosine triphosphate (ATP). If a substance must move into the cell against its concentration gradient—that is, if the concentration of the substance inside the cell is greater than its concentration in the extracellular fluid (and vice versa)—the cell must use energy to move the substance. Some active transport mechanisms move small-molecular weight materials, such as ions, through the membrane. Other mechanisms transport much larger molecules

Electrochemical Gradient

We have discussed simple concentration gradients—differential concentrations of a substance across a space or a membrane—but in living systems, gradients are more complex. Because ions move into and out of cells and because cells contain proteins that do not move across the membrane and are mostly negatively charged, there is also an electrical gradient, a difference of charge, across the plasma membrane. The interior of living cells is electrically negative with respect to the extracellular fluid in which they are bathed, and at the same time, cells have higher concentrations of potassium (K^+) and lower concentrations of sodium (Na^+) than does the extracellular fluid. So in a living cell, the concentration gradient of Na^+ tends to drive it into the cell, and the electrical gradient of Na^+ (a positive ion) also tends to drive it inward to the negatively charged interior. The situation is more complex, however, for other elements such as potassium. The electrical gradient of K^+ , a positive ion, also tends to drive it into the cell, but the concentration gradient of K^+ tends to drive K^+ out of the cell ([\[link\]](#)). The combined gradient of concentration and electrical charge that affects an ion is called its **electrochemical gradient**.

Note:

Art Connection



Electrochemical gradients arise from the combined effects of concentration gradients and electrical gradients. (credit: "Synaptitude"/Wikimedia Commons)

Injection of a potassium solution into a person's blood is lethal; this is used in capital punishment and euthanasia. Why do you think a potassium solution injection is lethal?

Moving Against a Gradient

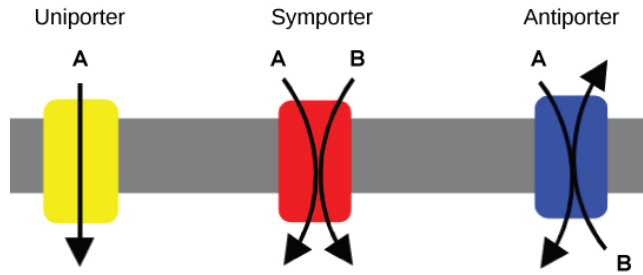
To move substances against a concentration or electrochemical gradient, the cell must use energy. This energy is harvested from ATP generated through the cell's metabolism. Active transport mechanisms, collectively called

pumps, work against electrochemical gradients. Small substances constantly pass through plasma membranes. Active transport maintains concentrations of ions and other substances needed by living cells in the face of these passive movements. Much of a cell's supply of metabolic energy may be spent maintaining these processes. (Most of a red blood cell's metabolic energy is used to maintain the imbalance between exterior and interior sodium and potassium levels required by the cell.) Because active transport mechanisms depend on a cell's metabolism for energy, they are sensitive to many metabolic poisons that interfere with the supply of ATP.

Two mechanisms exist for the transport of small-molecular weight material and small molecules. **Primary active transport** moves ions across a membrane and creates a difference in charge across that membrane, which is directly dependent on ATP. **Secondary active transport** describes the movement of material that is due to the electrochemical gradient established by primary active transport that does not directly require ATP.

Carrier Proteins for Active Transport

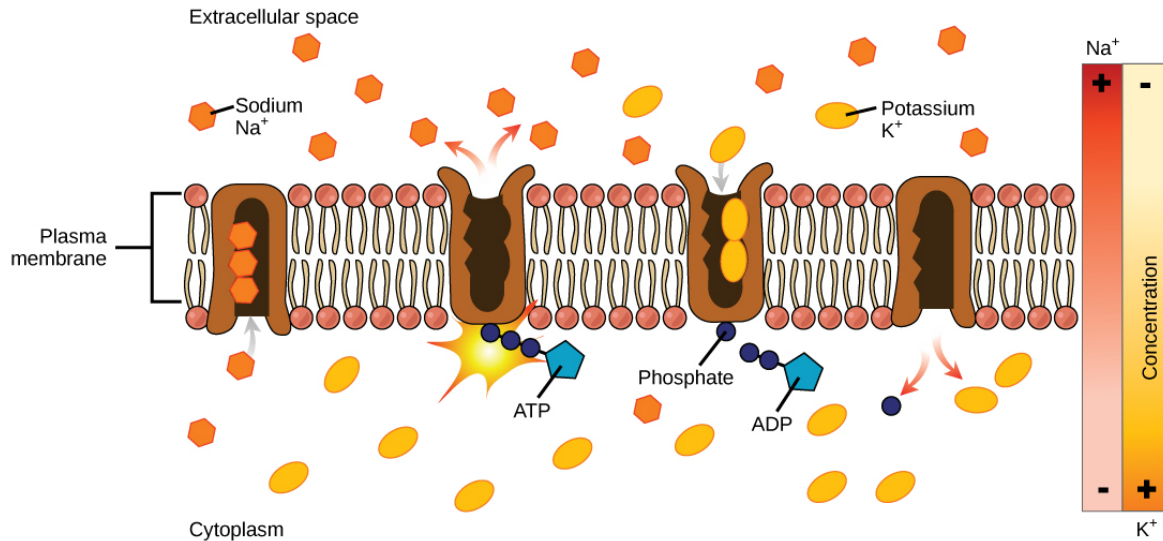
An important membrane adaption for active transport is the presence of specific carrier proteins or pumps to facilitate movement: there are three types of these proteins or **transporters** ([\[link\]](#)). A **uniporter** carries one specific ion or molecule. A **symporter** carries two different ions or molecules, both in the same direction. An **antiporter** also carries two different ions or molecules, but in different directions. All of these transporters can also transport small, uncharged organic molecules like glucose. These three types of carrier proteins are also found in facilitated diffusion, but they do not require ATP to work in that process. Some examples of pumps for active transport are $\text{Na}^+\text{-K}^+$ ATPase, which carries sodium and potassium ions, and $\text{H}^+\text{-K}^+$ ATPase, which carries hydrogen and potassium ions. Both of these are antiporter carrier proteins. Two other carrier proteins are Ca^{2+} ATPase and H^+ ATPase, which carry only calcium and only hydrogen ions, respectively. Both are pumps.



A uniporter carries one molecule or ion. A symporter carries two different molecules or ions, both in the same direction. An antiporter also carries two different molecules or ions, but in different directions. (credit: modification of work by “Lupask”/Wikimedia Commons)

Primary Active Transport

The primary active transport that functions with the active transport of sodium and potassium allows secondary active transport to occur. The second transport method is still considered active because it depends on the use of energy as does primary transport ([link](#)).



Primary active transport moves ions across a membrane, creating an electrochemical gradient (electrogenic transport). (credit: modification of work by Mariana Ruiz Villareal)

One of the most important pumps in animal cells is the sodium-potassium pump (Na⁺-K⁺ ATPase), which maintains the electrochemical gradient (and the correct concentrations of Na⁺ and K⁺) in living cells. The sodium-potassium pump moves K⁺ into the cell while moving Na⁺ out at the same time, at a ratio of three Na⁺ for every two K⁺ ions moved in. The Na⁺-K⁺ ATPase exists in two forms, depending on its orientation to the interior or exterior of the cell and its affinity for either sodium or potassium ions. The process consists of the following six steps.

1. With the enzyme oriented towards the interior of the cell, the carrier has a high affinity for sodium ions. Three ions bind to the protein.
2. ATP is hydrolyzed by the protein carrier and a low-energy phosphate group attaches to it.
3. As a result, the carrier changes shape and re-orientates itself towards the exterior of the membrane. The protein's affinity for sodium decreases and the three sodium ions leave the carrier.
4. The shape change increases the carrier's affinity for potassium ions, and two such ions attach to the protein. Subsequently, the low-energy

- phosphate group detaches from the carrier.
5. With the phosphate group removed and potassium ions attached, the carrier protein repositions itself towards the interior of the cell.
 6. The carrier protein, in its new configuration, has a decreased affinity for potassium, and the two ions are released into the cytoplasm. The protein now has a higher affinity for sodium ions, and the process starts again.

Several things have happened as a result of this process. At this point, there are more sodium ions outside of the cell than inside and more potassium ions inside than out. For every three ions of sodium that move out, two ions of potassium move in. This results in the interior being slightly more negative relative to the exterior. This difference in charge is important in creating the conditions necessary for the secondary process. The sodium-potassium pump is, therefore, an **electrogenic pump** (a pump that creates a charge imbalance), creating an electrical imbalance across the membrane and contributing to the membrane potential.

Note:

Link to Learning



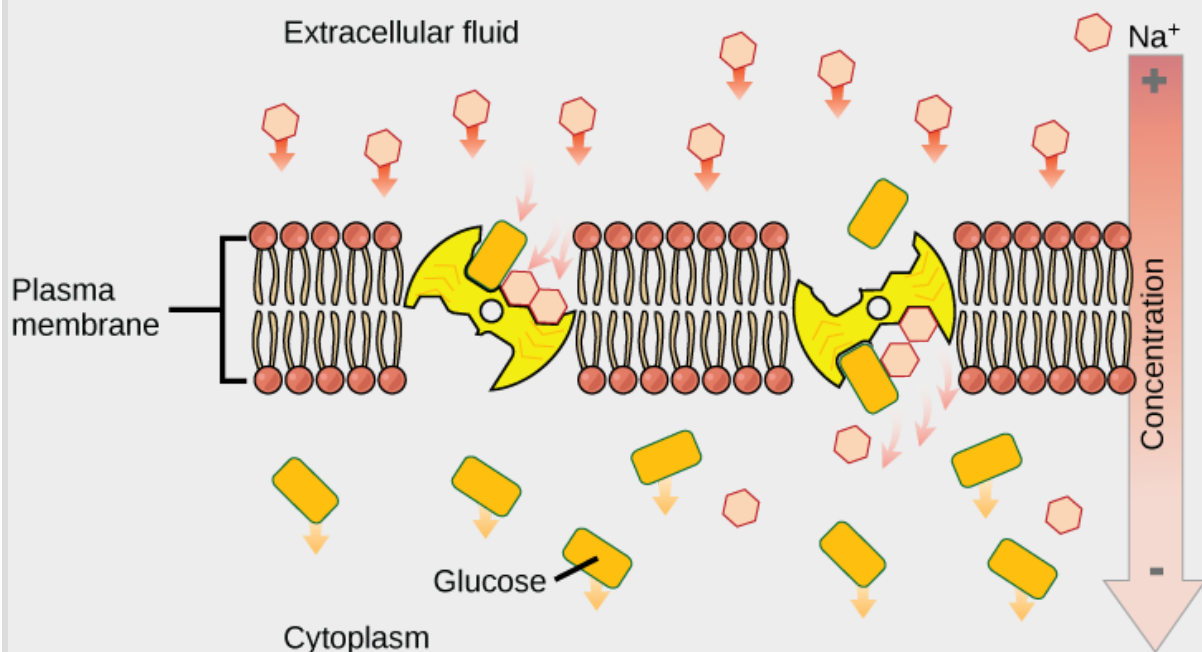
Visit the [site](#) to see a simulation of active transport in a sodium-potassium ATPase.

Secondary Active Transport (Co-transport)

Secondary active transport brings sodium ions, and possibly other compounds, into the cell. As sodium ion concentrations build outside of the plasma membrane because of the action of the primary active transport process, an electrochemical gradient is created. If a channel protein exists and is open, the sodium ions will be pulled through the membrane. This movement is used to transport other substances that can attach themselves to the transport protein through the membrane ([\[link\]](#)). Many amino acids, as well as glucose, enter a cell this way. This secondary process is also used to store high-energy hydrogen ions in the mitochondria of plant and animal cells for the production of ATP. The potential energy that accumulates in the stored hydrogen ions is translated into kinetic energy as the ions surge through the channel protein ATP synthase, and that energy is used to convert ADP into ATP.

Note:

Art Connection



An electrochemical gradient, created by primary active transport, can move other substances against their concentration gradients, a process called co-transport or secondary active transport. (credit: modification of work by Mariana Ruiz Villareal)

If the pH outside the cell decreases, would you expect the amount of amino acids transported into the cell to increase or decrease?

Section Summary

The combined gradient that affects an ion includes its concentration gradient and its electrical gradient. A positive ion, for example, might tend to diffuse into a new area, down its concentration gradient, but if it is diffusing into an area of net positive charge, its diffusion will be hampered by its electrical gradient. When dealing with ions in aqueous solutions, a combination of the electrochemical and concentration gradients, rather than just the concentration gradient alone, must be considered. Living cells need certain substances that exist inside the cell in concentrations greater than they exist in the extracellular space. Moving substances up their electrochemical gradients requires energy from the cell. Active transport uses energy stored in ATP to fuel this transport. Active transport of small molecular-sized materials uses integral proteins in the cell membrane to move the materials: These proteins are analogous to pumps. Some pumps, which carry out primary active transport, couple directly with ATP to drive their action. In co-transport (or secondary active transport), energy from primary transport can be used to move another substance into the cell and up its concentration gradient.

Art Connections

Exercise:

Problem:

[\[link\]](#) Injection of a potassium solution into a person's blood is lethal; this is used in capital punishment and euthanasia. Why do you think a potassium solution injection is lethal?

Solution:

[\[link\]](#) Cells typically have a high concentration of potassium in the cytoplasm and are bathed in a high concentration of sodium. Injection of potassium dissipates this electrochemical gradient. In heart muscle, the sodium/potassium potential is responsible for transmitting the signal that causes the muscle to contract. When this potential is dissipated, the signal can't be transmitted, and the heart stops beating. Potassium injections are also used to stop the heart from beating during surgery.

Exercise:

Problem:

[\[link\]](#) If the pH outside the cell decreases, would you expect the amount of amino acids transported into the cell to increase or decrease?

Solution:

[\[link\]](#) A decrease in pH means an increase in positively charged H^+ ions, and an increase in the electrical gradient across the membrane. The transport of amino acids into the cell will increase.

Review Questions

Exercise:

Problem:

Active transport must function continuously because _____.

- a. plasma membranes wear out
 - b. not all membranes are amphiphilic
 - c. facilitated transport opposes active transport
 - d. diffusion is constantly moving solutes in opposite directions
-

Solution:

D

Exercise:

Problem:

How does the sodium-potassium pump make the interior of the cell negatively charged?

- a. by expelling anions
 - b. by pulling in anions
 - c. by expelling more cations than are taken in
 - d. by taking in and expelling an equal number of cations
-

Solution:

C

Exercise:

Problem:

What is the combination of an electrical gradient and a concentration gradient called?

- a. potential gradient
 - b. electrical potential
 - c. concentration potential
 - d. electrochemical gradient
-

Solution:

D

Free Response

Exercise:

Problem:

Where does the cell get energy for active transport processes?

Solution:

The cell harvests energy from ATP produced by its own metabolism to power active transport processes, such as the activity of pumps.

Exercise:**Problem:**

How does the sodium-potassium pump contribute to the net negative charge of the interior of the cell?

Solution:

The sodium-potassium pump forces out three (positive) Na^+ ions for every two (positive) K^+ ions it pumps in, thus the cell loses a positive charge at every cycle of the pump.

Glossary

active transport

method of transporting material that requires energy

antiporter

transporter that carries two ions or small molecules in different directions

electrochemical gradient

gradient produced by the combined forces of an electrical gradient and a chemical gradient

electrogenic pump

pump that creates a charge imbalance

primary active transport

active transport that moves ions or small molecules across a membrane and may create a difference in charge across that membrane

pump

active transport mechanism that works against electrochemical gradients

secondary active transport

movement of material that is due to the electrochemical gradient established by primary active transport

symporter

transporter that carries two different ions or small molecules, both in the same direction

transporter

specific carrier proteins or pumps that facilitate movement

uniporter

transporter that carries one specific ion or molecule

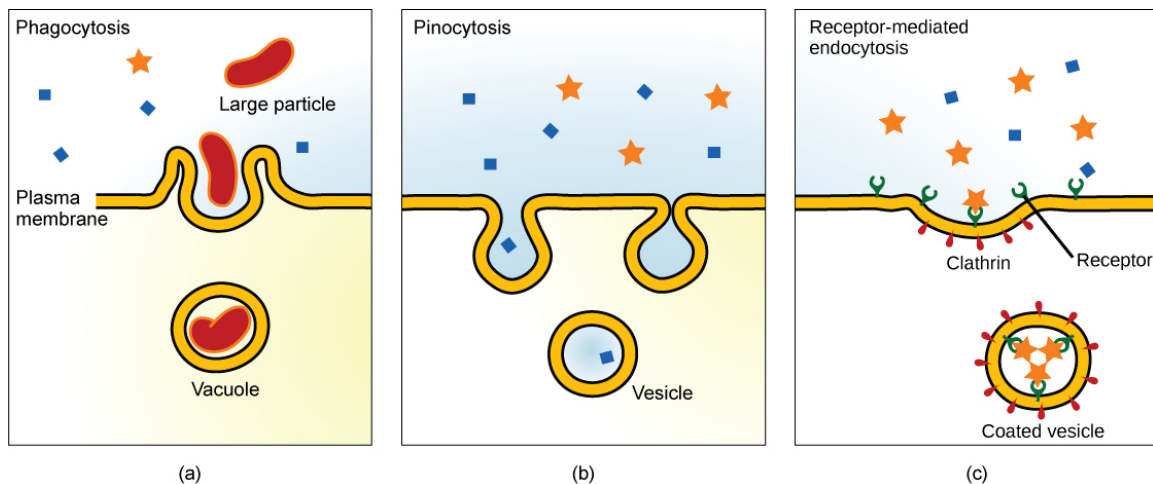
Bis2A 09.3 Endocytosis

By the end of this section, you will be able to:

- Understand how electrochemical gradients affect ions
- Describe endocytosis, including phagocytosis, pinocytosis, and receptor-mediated endocytosis
- Understand the process of exocytosis

Endocytosis

Endocytosis is a type of active transport that moves particles, such as large molecules, parts of cells, and even whole cells, into a cell. There are different variations of endocytosis, but all share a common characteristic: The plasma membrane of the cell invaginates, forming a pocket around the target particle. The pocket pinches off, resulting in the particle being contained in a newly created vacuole that is formed from the plasma membrane.



Three variations of endocytosis are shown. (a) In one form of endocytosis, phagocytosis, the cell membrane surrounds the particle and pinches off to form an intracellular vacuole. (b) In another type of endocytosis, pinocytosis, the cell membrane surrounds a small volume of fluid and pinches off, forming a vesicle. (c) In receptor-mediated endocytosis, uptake of substances

by the cell is targeted to a single type of substance that binds at the receptor on the external cell membrane. (credit: modification of work by Mariana Ruiz Villarreal)

Phagocytosis is the process by which large particles, such as cells, are taken in by a cell. For example, when microorganisms invade the human body, a type of white blood cell called a neutrophil removes the invader through this process, surrounding and engulfing the microorganism, which is then destroyed by the neutrophil ([\[link\]](#)).

A variation of endocytosis is called **pinocytosis**. This literally means “cell drinking” and was named at a time when the assumption was that the cell was purposefully taking in extracellular fluid. In reality, this process takes in solutes that the cell needs from the extracellular fluid ([\[link\]](#)).

A targeted variation of endocytosis employs binding proteins in the plasma membrane that are specific for certain substances ([\[link\]](#)). The particles bind to the proteins and the plasma membrane invaginates, bringing the substance and the proteins into the cell. If passage across the membrane of the target of **receptor-mediated endocytosis** is ineffective, it will not be removed from the tissue fluids or blood. Instead, it will stay in those fluids and increase in concentration. Some human diseases are caused by a failure of receptor-mediated endocytosis. For example, the form of cholesterol termed low-density lipoprotein or LDL (also referred to as “bad” cholesterol) is removed from the blood by receptor-mediated endocytosis. In the human genetic disease familial hypercholesterolemia, the LDL receptors are defective or missing entirely. People with this condition have life-threatening levels of cholesterol in their blood, because their cells cannot clear the chemical from their blood.

Note:

Concept in Action

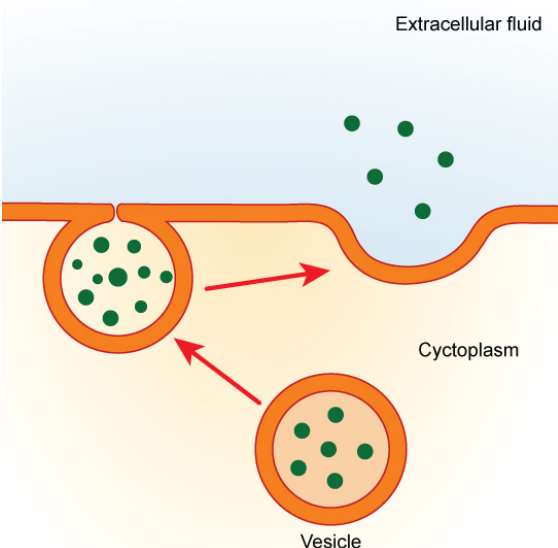


See receptor-mediated endocytosis in action and click on different parts for a focused [animation](#) to learn more.

Exocytosis

In contrast to these methods of moving material into a cell is the process of exocytosis. **Exocytosis** is the opposite of the processes discussed above in that its purpose is to expel material from the cell into the extracellular fluid. A particle enveloped in membrane fuses with the interior of the plasma membrane. This fusion opens the membranous envelope to the exterior of the cell, and the particle is expelled into the extracellular space ([\[link\]](#)).

Exocytosis



In exocytosis, a vesicle

migrates to the plasma membrane, binds, and releases its contents to the outside of the cell. (credit: modification of work by Mariana Ruiz Villarreal)

Section Summary

The combined gradient that affects an ion includes its concentration gradient and its electrical gradient. Living cells need certain substances in concentrations greater than they exist in the extracellular space. Moving substances up their electrochemical gradients requires energy from the cell. Active transport uses energy stored in ATP to fuel the transport. Active transport of small molecular-size material uses integral proteins in the cell membrane to move the material—these proteins are analogous to pumps. Some pumps, which carry out primary active transport, couple directly with ATP to drive their action. In secondary transport, energy from primary transport can be used to move another substance into the cell and up its concentration gradient.

Endocytosis methods require the direct use of ATP to fuel the transport of large particles such as macromolecules; parts of cells or whole cells can be engulfed by other cells in a process called phagocytosis. In phagocytosis, a portion of the membrane invaginates and flows around the particle, eventually pinching off and leaving the particle wholly enclosed by an envelope of plasma membrane. Vacuoles are broken down by the cell, with the particles used as food or dispatched in some other way. Pinocytosis is a similar process on a smaller scale. The cell expels waste and other particles through the reverse process, exocytosis. Wastes are moved outside the cell, pushing a membranous vesicle to the plasma membrane, allowing the vesicle to fuse with the membrane and incorporating itself into the membrane structure, releasing its contents to the exterior of the cell.

Multiple Choice

Exercise:

Problem:

Active transport must function continuously because _____.

- a. plasma membranes wear out
- b. cells must be in constant motion
- c. facilitated transport opposes active transport
- d. diffusion is constantly moving the solutes in the other direction

Solution:

D

Free Response

Exercise:

Problem:

Where does the cell get energy for active transport processes?

Solution:

The cell harvests energy from ATP produced by its own metabolism to power active transport processes, such as pumps.

Glossary

active transport

the method of transporting material that requires energy

electrochemical gradient

a gradient produced by the combined forces of the electrical gradient and the chemical gradient

endocytosis

a type of active transport that moves substances, including fluids and particles, into a cell

exocytosis

a process of passing material out of a cell

phagocytosis

a process that takes macromolecules that the cell needs from the extracellular fluid; a variation of endocytosis

pinocytosis

a process that takes solutes that the cell needs from the extracellular fluid; a variation of endocytosis

receptor-mediated endocytosis

a variant of endocytosis that involves the use of specific binding proteins in the plasma membrane for specific molecules or particles

Bis2A 10.0 Prokaryotes: Bacteria and Archaea

By the end of this section, you will be able to:

- List the unifying characteristics of bacteria and archaea
- Describe what scientists know about the origins of bacteria and archaea
- Explain the difference between bacteria and archaea and why they are collectively referred to as prokaryotes

Introduction

"Perhaps bacteria may tentatively be regarded as biochemical experiments; owing to their relatively small size and rapid growth, variations must arise much more frequently than in more differentiated forms of life, and they can in addition afford to occupy more precarious positions in natural economy than larger organisms with more exacting requirements." Marjory Stephenson, in *Bacterial Metabolism*, (1930)

Prokaryotic Diversity

Prokaryotes are ubiquitous, and, as mentioned above, highly diverse in their metabolic activities. They cover every imaginable surface where there is sufficient moisture, and they live on and inside of other living things. In the typical human body, prokaryotic cells outnumber human body cells by about ten to one. They comprise the majority of living things in all ecosystems. Some prokaryotes thrive in environments that are inhospitable for most living things. Prokaryotes recycle **nutrients**—essential substances (such as carbon and nitrogen)—and they drive the evolution of new ecosystems, some of which are natural and others man-made. Prokaryotes have been on Earth since long before multicellular life appeared.

Prokaryotes, the First Inhabitants of Earth

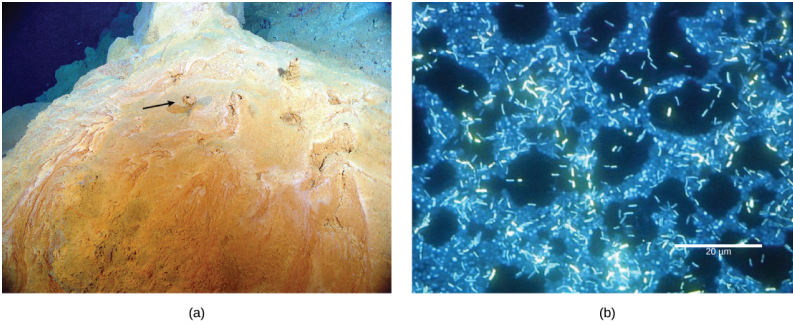
When and where did life begin? What were the conditions on Earth when life began? Prokaryotes were the first forms of life on Earth, and they existed for billions of years before plants and animals appeared. The Earth and its moon are thought to be about 4.54 billion years old. This estimate is based on evidence from radiometric dating of meteorite material together

with other substrate material from Earth and the moon. Early Earth had a very different atmosphere (contained less molecular oxygen) than it does today and was subjected to strong radiation; thus, the first organisms would have flourished where they were more protected, such as in ocean depths or beneath the surface of the Earth. At this time too, strong volcanic activity was common on Earth, so it is likely that these first organisms—the first prokaryotes—were adapted to very high temperatures. Early Earth was prone to geological upheaval and volcanic eruption, and was subject to bombardment by mutagenic radiation from the sun. The first organisms were prokaryotes that could withstand these harsh conditions.

Microbial Mats

Microbial mats or large biofilms may represent the earliest forms of life on Earth; there is fossil evidence of their presence starting about 3.5 billion years ago. A **microbial mat** is a multi-layered sheet of prokaryotes ([\[link\]](#)) that includes mostly bacteria, but also archaea. Microbial mats are a few centimeters thick, and they typically grow where different types of materials interface, mostly on moist surfaces. The various types of prokaryotes that comprise them carry out different metabolic pathways, and that is the reason for their various colors. Prokaryotes in a microbial mat are held together by a glue-like sticky substance that they secrete called extracellular matrix.

The first microbial mats likely obtained their energy from chemicals found near hydrothermal vents. A **hydrothermal vent** is a breakage or fissure in the Earth's surface that releases geothermally heated water. With the evolution of photosynthesis about 3 billion years ago, some prokaryotes in microbial mats came to use a more widely available energy source—sunlight—whereas others were still dependent on chemicals from hydrothermal vents for energy and food.



This (a) microbial mat, about one meter in diameter, grows over a hydrothermal vent in the Pacific Ocean in a region known as the “Pacific Ring of Fire.” The mat helps retain microbial nutrients. Chimneys such as the one indicated by the arrow allow gases to escape. (b) In this micrograph, bacteria are visualized using fluorescence microscopy. (credit a: modification of work by Dr. Bob Embley, NOAA PMEL, Chief Scientist; credit b: modification of work by Ricardo Murga, Rodney Donlan, CDC; scale-bar data from Matt Russell)

Stromatolites

Fossilized microbial mats represent the earliest record of life on Earth. A **stromatolite** is a sedimentary structure formed when minerals precipitate out of water by prokaryotes in a microbial mat ([\[link\]](#)). Stromatolites form layered rocks made of carbonate or silicate. Although most stromatolites are artifacts from the past, there are places on Earth where stromatolites are still forming. For example, growing stromatolites have been found in the Anza-Borrego Desert State Park in San Diego County, California.



(a)



(b)

(a) These living stromatolites are located in Shark Bay, Australia. (b) These fossilized stromatolites, found in Glacier National Park, Montana, are nearly 1.5 billion years old. (credit a: Robert Young; credit b: P. Carrara, NPS)

The Ancient Atmosphere

Evidence indicates that during the first two billion years of Earth's existence, the atmosphere was **anoxic**, meaning that there was no molecular oxygen. Therefore, only those organisms that can grow without oxygen—**anaerobic** organisms—were able to live. Autotrophic organisms that convert solar energy into chemical energy are called **phototrophs**, and they appeared within one billion years of the formation of Earth. Then, **cyanobacteria**, also known as blue-green algae, evolved from these simple phototrophs one billion years later. Cyanobacteria ([link](#)) began the oxygenation of the atmosphere. Increased atmospheric oxygen allowed the development of more efficient O₂-utilizing catabolic pathways. It also opened up the land to increased colonization, because some O₂ is converted into O₃ (ozone) and ozone effectively absorbs the ultraviolet light that would otherwise cause lethal mutations in DNA. Ultimately, the increase in O₂ concentrations allowed the evolution of other life forms.



This hot spring in Yellowstone National Park flows toward the foreground. Cyanobacteria in the spring are green, and as water flows down the gradient, the intensity of the color increases as cell density increases. The water is cooler at the edges of the stream than in the center, causing the edges to appear greener. (credit: Graciela Brelles-Mariño)

Microbes Are Adaptable: Life in Moderate and Extreme Environments

Some organisms have developed strategies that allow them to survive harsh conditions. Prokaryotes thrive in a vast array of environments: Some grow in conditions that would seem very normal to us, whereas others are able to thrive and grow under conditions that would kill a plant or animal. Almost all prokaryotes have a cell wall, a protective structure that allows them to survive in both hyper- and hypo-osmotic conditions. Some soil bacteria are able to form endospores that resist heat and drought, thereby allowing the

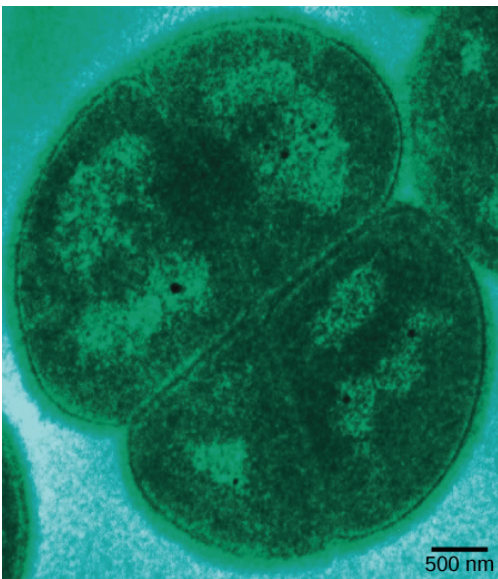
organism to survive until favorable conditions recur. These adaptations, along with others, allow bacteria to be the most abundant life form in all terrestrial and aquatic ecosystems.

Other bacteria and archaea are adapted to grow under extreme conditions and are called **extremophiles**, meaning “lovers of extremes.”

Extremophiles have been found in all kinds of environments: the depth of the oceans, hot springs, the Arctic and the Antarctic, in very dry places, deep inside Earth, in harsh chemical environments, and in high radiation environments ([\[link\]](#)), just to mention a few. These organisms give us a better understanding of prokaryotic diversity and open up the possibility of finding new prokaryotic species that may lead to the discovery of new therapeutic drugs or have industrial applications. Because they have specialized adaptations that allow them to live in extreme conditions, many extremophiles cannot survive in moderate environments. There are many different groups of extremophiles: They are identified based on the conditions in which they grow best, and several habitats are extreme in multiple ways. For example, a soda lake is both salty and alkaline, so organisms that live in a soda lake must be both alkaliphiles and halophiles ([\[link\]](#)). Other extremophiles, like **radioresistant** organisms, do not prefer an extreme environment (in this case, one with high levels of radiation), but have adapted to survive in it ([\[link\]](#)).

Extremophiles and Their Preferred Conditions	
Extremophile Type	Conditions for Optimal Growth
Acidophiles	pH 3 or below
Alkaliphiles	pH 9 or above
Thermophiles	Temperature 60–80 °C (140–176 °F)

Extremophiles and Their Preferred Conditions	
Extremophile Type	Conditions for Optimal Growth
Hyperthermophiles	Temperature 80–122 °C (176–250 °F)
Psychrophiles	Temperature of -15 °C (5 °F) or lower
Halophiles	Salt concentration of at least 0.2 M
Osmophiles	High sugar concentration



Deinococcus radiodurans, visualized in this false color transmission electron micrograph, is a prokaryote that can tolerate very high doses of ionizing radiation. It has developed DNA

repair mechanisms that allow it to reconstruct its chromosome even if it has been broken into hundreds of pieces by radiation or heat. (credit: modification of work by Michael Daly; scale-bar data from Matt Russell)

Antibiotics: Are We Facing a Crisis?

The word *antibiotic* comes from the Greek *anti* meaning “against” and *bios* meaning “life.” An **antibiotic** is a chemical, produced either by microbes or synthetically, that is hostile to the growth of other organisms. Today’s news and media often address concerns about an antibiotic crisis. Are the antibiotics that easily treated bacterial infections in the past becoming obsolete? Are there new “superbugs”—bacteria that have evolved to become more resistant to our arsenal of antibiotics? Is this the beginning of the end of antibiotics? All these questions challenge the healthcare community.

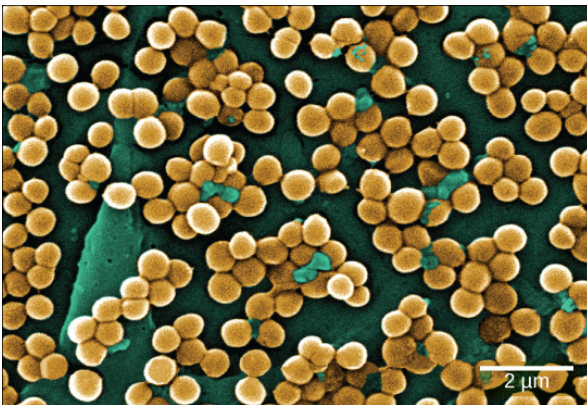
One of the main causes of resistant bacteria is the abuse of antibiotics. The imprudent and excessive use of antibiotics has resulted in the natural selection of resistant forms of bacteria. The antibiotic kills most of the infecting bacteria, and therefore only the resistant forms remain. These resistant forms reproduce, resulting in an increase in the proportion of resistant forms over non-resistant ones. Another major misuse of antibiotics is in patients with colds or the flu, for which antibiotics are useless. Another problem is the excessive use of antibiotics in livestock. The routine use of antibiotics in animal feed promotes bacterial resistance as well. In the United States, 70 percent of the antibiotics produced are fed to animals. These antibiotics are given to livestock in low doses, which maximize the probability of resistance developing, and these resistant bacteria are readily transferred to humans.

One of the Superbugs: MRSA

The imprudent use of antibiotics has paved the way for bacteria to expand populations of resistant forms. For example, *Staphylococcus aureus*, often called “staph,” is a common bacterium that can live in the human body and is usually easily treated with antibiotics. A very dangerous strain, however, **methicillin-resistant *Staphylococcus aureus* (MRSA)** has made the news over the past few years ([\[link\]](#)). This strain is resistant to many commonly used antibiotics, including methicillin, amoxicillin, penicillin, and oxacillin. MRSA can cause infections of the skin, but it can also infect the bloodstream, lungs, urinary tract, or sites of injury. While MRSA infections are common among people in healthcare facilities, they have also appeared in healthy people who haven’t been hospitalized but who live or work in tight populations (like military personnel and prisoners). Researchers have expressed concern about the way this latter source of MRSA targets a much younger population than those residing in care facilities. *The Journal of the American Medical Association* reported that, among MRSA-afflicted persons in healthcare facilities, the average age is 68, whereas people with “community-associated MRSA” (CA-MRSA) have an average age of 23.

[\[footnote\]](#)

Naimi, TS, LeDell, KH, Como-Sabetti, K, et al. Comparison of community- and health care-associated methicillin-resistant *Staphylococcus aureus* infection. *JAMA* 290 (2003): 2976–84, [doi: 10.1001/jama.290.22.2976](#).



This scanning electron
micrograph shows methicillin-

resistant *Staphylococcus aureus* bacteria, commonly known as MRSA. *S. Aureus* is not always pathogenic, but can cause diseases such as food poisoning and skin and respiratory infections. (credit: modification of work by Janice Haney Carr; scale-bar data from Matt Russell)

In summary, the medical community is facing an antibiotic crisis. Some scientists believe that after years of being protected from bacterial infections by antibiotics, we may be returning to a time in which a simple bacterial infection could again devastate the human population. Researchers are developing new antibiotics, but it takes many years to of research and clinical trials, plus financial investments in the millions of dollars, to generate an effective and approved drug.

Foodborne Diseases

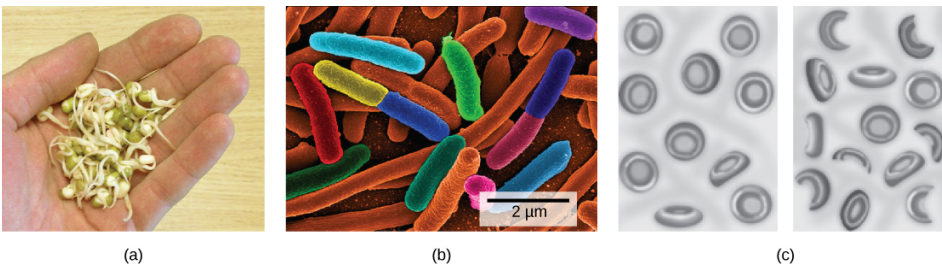
Prokaryotes are everywhere: They readily colonize the surface of any type of material, and food is not an exception. Most of the time, prokaryotes colonize food and food-processing equipment in the form of a biofilm. Outbreaks of bacterial infection related to food consumption are common. A **foodborne disease** (colloquially called “food poisoning”) is an illness resulting from the consumption of contaminated food, or the pathogenic bacteria, viruses, or other parasites that contaminate food. Although the United States has one of the safest food supplies in the world, the U.S. Centers for Disease Control and Prevention (CDC) has reported that “76 million people get sick, more than 300,000 are hospitalized, and 5,000 Americans die each year from foodborne illness.”

The characteristics of foodborne illnesses have changed over time. In the past, it was relatively common to hear about sporadic cases of **botulism**, the

potentially fatal disease produced by a toxin from the anaerobic bacterium *Clostridium botulinum*. Some of the most common sources for this bacterium were non-acidic canned foods, homemade pickles, and processed meat and sausages. The can, jar, or package created a suitable anaerobic environment where *Clostridium* could grow. Proper sterilization and canning procedures have reduced the incidence of this disease.

While people may tend to think of foodborne illnesses as associated with animal-based foods, most cases are now linked to produce. There have been serious, produce-related outbreaks associated with raw spinach in the United States and with vegetable sprouts in Germany, and these types of outbreaks have become more common. The raw spinach outbreak in 2006 was produced by the bacterium *E. coli* serotype O157:H7. A **serotype** is a strain of bacteria that carries a set of similar antigens on its cell surface, and there are often many different serotypes of a bacterial species. Most *E. coli* are not particularly dangerous to humans, but serotype O157:H7 can cause bloody diarrhea and is potentially fatal.

All types of food can potentially be contaminated with bacteria. Recent outbreaks of *Salmonella* reported by the CDC occurred in foods as diverse as peanut butter, alfalfa sprouts, and eggs. A deadly outbreak in Germany in 2010 was caused by *E. coli* contamination of vegetable sprouts ([\[link\]](#)). The strain that caused the outbreak was found to be a new serotype not previously involved in other outbreaks, which indicates that *E. coli* is continuously evolving.



(a) Vegetable sprouts grown at an organic farm were the cause of an (b) *E. coli* outbreak that killed 32 people and sickened 3,800 in Germany in 2011. The

strain responsible, *E. coli* O104:H4, produces Shiga toxin, a substance that inhibits protein synthesis in the host cell. The toxin (c) destroys red blood cells resulting in bloody diarrhea. Deformed red blood cells clog the capillaries of the kidney, which can lead to kidney failure, as happened to 845 patients in the 2011 outbreak. Kidney failure is usually reversible, but some patients experience kidney problems years later. (credit c: NIDDK, NIH)

Beneficial Bacteria

Not all prokaryotes are pathogenic. On the contrary, pathogens represent only a very small percentage of the diversity of the microbial world. In fact, our life would not be possible without prokaryotes. Just think about the role of prokaryotes in biogeochemical cycles.

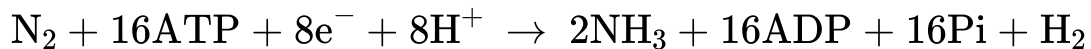
Cooperation between Bacteria and Eukaryotes: Nitrogen Fixation

Nitrogen is a very important element to living things, because it is part of nucleotides and amino acids that are the building blocks of nucleic acids and proteins, respectively. Nitrogen is usually the most limiting element in terrestrial ecosystems, with atmospheric nitrogen, N_2 , providing the largest pool of available nitrogen. However, eukaryotes cannot use atmospheric, gaseous nitrogen to synthesize macromolecules. Fortunately, nitrogen can be “fixed,” meaning it is converted into ammonia (NH_3) either biologically or abiotically. Abiotic nitrogen fixation occurs as a result of lightning or by industrial processes.

Biological nitrogen fixation (BNF) is exclusively carried out by prokaryotes: soil bacteria, cyanobacteria, and *Frankia* spp. (filamentous bacteria interacting with actinorhizal plants such as alder, bayberry, and sweet fern). After photosynthesis, BNF is the second most important

biological process on Earth. The equation representing the process is as follows

Equation:



where Pi stands for inorganic phosphate. The total fixed nitrogen through BNF is about 100 to 180 million metric tons per year. Biological processes contribute 65 percent of the nitrogen used in agriculture.

Cyanobacteria are the most important nitrogen fixers in aquatic environments. In soil, members of the genus *Clostridium* are examples of free-living, nitrogen-fixing bacteria. Other bacteria live symbiotically with legume plants, providing the most important source of BNF. Symbionts may fix more nitrogen in soils than free-living organisms by a factor of 10. Soil bacteria, collectively called rhizobia, are able to symbiotically interact with legumes to form **nodules**, specialized structures where nitrogen fixation occurs ([\[link\]](#)). Nitrogenase, the enzyme that fixes nitrogen, is inactivated by oxygen, so the nodule provides an oxygen-free area for nitrogen fixation to take place. This process provides a natural and inexpensive plant fertilizer, as it reduces atmospheric nitrogen into ammonia, which is easily usable by plants. The use of legumes is an excellent alternative to chemical fertilization and is of special interest to sustainable agriculture, which seeks to minimize the use of chemicals and conserve natural resources. Through symbiotic nitrogen fixation, the plant benefits from using an endless source of nitrogen: the atmosphere. Bacteria benefit from using photosynthates (carbohydrates produced during photosynthesis) from the plant and having a protected niche. Additionally, the soil benefits from being naturally fertilized. Therefore, the use of rhizobia as biofertilizers is a sustainable practice.

Why are legumes so important? Some, like soybeans, are key sources of agricultural protein. Some of the most important grain legumes are soybean, peanuts, peas, chickpeas, and beans. Other legumes, such as alfalfa, are used to feed cattle.



Soybean (*Glycine max*) is a legume that interacts symbiotically with the soil bacterium *Bradyrhizobium japonicum* to form specialized structures on the roots called nodules where nitrogen fixation occurs. (credit: USDA)

Early Biotechnology: Cheese, Bread, Wine, Beer, and Yogurt

According to the United Nations Convention on Biological Diversity, **biotechnology** is “any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use.”^{[[footnote](#)]} The concept of “specific use” involves some sort of commercial application. Genetic engineering, artificial selection, antibiotic production, and cell culture are current topics of study in biotechnology. However, humans have used prokaryotes before the term biotechnology was even coined. In addition, some of the goods and services are as simple as cheese, bread, wine, beer, and yogurt, which employ both bacteria and other microbes, such as yeast, a fungus ([link](#)). <http://www.cbd.int/convention/articles/?a=cbd-02>, United Nations Convention on Biological Diversity: Article 2: Use of Terms.



(a)



(b)



(c)



(d)

Some of the products derived from the use of prokaryotes in early biotechnology include (a) cheese, (b) wine, (c) beer and bread, and (d) yogurt.

(credit bread: modification of work by F. Rodrigo/Wikimedia Commons; credit wine: modification of work by Jon Sullivan; credit beer and bread: modification of work by Kris Miller; credit yogurt: modification of work by Jon Sullivan)

Cheese production began around 4,000–7,000 years ago when humans began to breed animals and process their milk. Fermentation in this case preserves nutrients: Milk will spoil relatively quickly, but when processed as cheese, it is more stable. As for beer, the oldest records of brewing are about 6,000 years old and refer to the Sumerians. Evidence indicates that the Sumerians discovered fermentation by chance. Wine has been produced

for about 4,500 years, and evidence suggests that cultured milk products, like yogurt, have existed for at least 4,000 years.

Using Prokaryotes to Clean up Our Planet: Bioremediation

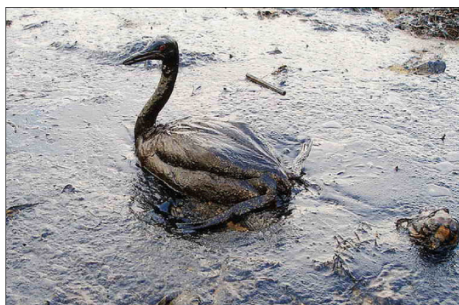
Microbial **bioremediation** is the use of prokaryotes (or microbial metabolism) to remove pollutants. Bioremediation has been used to remove agricultural chemicals (pesticides, fertilizers) that leach from soil into groundwater and the subsurface. Certain toxic metals and oxides, such as selenium and arsenic compounds, can also be removed from water by bioremediation. The reduction of SeO_4^{-2} to SeO_3^{-2} and to Se^0 (metallic selenium) is a method used to remove selenium ions from water. Mercury is an example of a toxic metal that can be removed from an environment by bioremediation. As an active ingredient of some pesticides, mercury is used in industry and is also a by-product of certain processes, such as battery production. Methyl mercury is usually present in very low concentrations in natural environments, but it is highly toxic because it accumulates in living tissues. Several species of bacteria can carry out the biotransformation of toxic mercury into nontoxic forms. These bacteria, such as *Pseudomonas aeruginosa*, can convert Hg^{+2} into Hg^0 , which is nontoxic to humans.

One of the most useful and interesting examples of the use of prokaryotes for bioremediation purposes is the cleanup of oil spills. The importance of prokaryotes to petroleum bioremediation has been demonstrated in several oil spills in recent years, such as the Exxon Valdez spill in Alaska (1989) ([link](#)), the Prestige oil spill in Spain (2002), the spill into the Mediterranean from a Lebanon power plant (2006), and more recently, the BP oil spill in the Gulf of Mexico (2010). To clean up these spills, bioremediation is promoted by the addition of inorganic nutrients that help bacteria to grow. Hydrocarbon-degrading bacteria feed on hydrocarbons in the oil droplet, breaking down the hydrocarbons. Some species, such as *Alcanivorax borkumensis*, produce surfactants that solubilize the oil, whereas other bacteria degrade the oil into carbon dioxide. In the case of oil spills in the ocean, ongoing, natural bioremediation tends to occur, inasmuch as there are oil-consuming bacteria in the ocean prior to the spill. In addition to naturally occurring oil-degrading bacteria, humans select and engineer bacteria that possess the same capability with increased efficacy

and spectrum of hydrocarbon compounds that can be processed. Under ideal conditions, it has been reported that up to 80 percent of the nonvolatile components in oil can be degraded within one year of the spill. Other oil fractions containing aromatic and highly branched hydrocarbon chains are more difficult to remove and remain in the environment for longer periods of time.



(a)



(b)

(a) Cleaning up oil after the Valdez spill in Alaska, workers hosed oil from beaches and then used a floating boom to corral the oil, which was finally skimmed from the water surface. Some species of bacteria are able to solubilize and degrade the oil. (b)

One of the most catastrophic consequences of oil spills is the damage to fauna. (credit a: modification of work by NOAA; credit b: modification of work by GOLUBENKOV, NGO: Saving Taman)

Note:

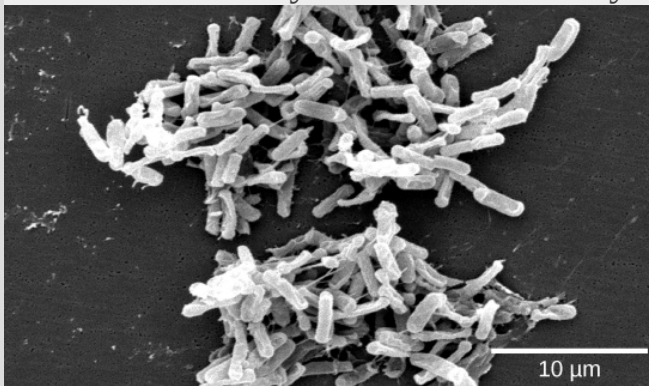
Everyday Connection

Microbes on the Human Body

The commensal bacteria that inhabit our skin and gastrointestinal tract do a host of good things for us. They protect us from pathogens, help us digest our food, and produce some of our vitamins and other nutrients. These

activities have been known for a long time. More recently, scientists have gathered evidence that these bacteria may also help regulate our moods, influence our activity levels, and even help control weight by affecting our food choices and absorption patterns. The Human Microbiome Project has begun the process of cataloging our normal bacteria (and archaea) so we can better understand these functions.

A particularly fascinating example of our normal flora relates to our digestive systems. People who take high numbers of antibiotics tend to lose many of their normal gut bacteria, allowing a naturally antibiotic-resistant species called *Clostridium difficile* to overgrow and cause severe gastric problems, especially chronic diarrhea ([link](#)). Obviously, trying to treat this problem with antibiotics only makes it worse. However, it has been successfully treated by giving the patients fecal transplants from healthy donors to reestablish the normal intestinal microbial community. Clinical trials are underway to ensure the safety and effectiveness of this technique.



This scanning electron micrograph shows *Clostridium difficile*, a Gram-positive, rod-shaped bacterium that causes severe diarrhea. Infection commonly occurs after the normal gut fauna is eradicated by antibiotics. (credit: modification of work by CDC, HHS; scale-bar data from Matt Russell)

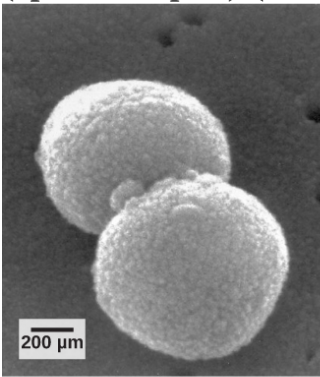
Scientists are also discovering that the absence of certain key microbes from our intestinal tract may set us up for a variety of problems. This seems to be particularly true regarding the appropriate functioning of the immune system. There are intriguing findings that suggest that the absence of these microbes is an important contributor to the development of allergies and some autoimmune disorders. Research is currently underway to test whether adding certain microbes to our internal ecosystem may help in the treatment of these problems as well as in treating some forms of autism.

Bis2A 10.1 Structure of Bacteria and Archaea

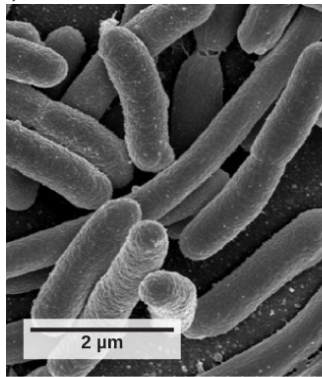
By the end of this section, you will be able to:

- Describe the basic structure of a typical prokaryote
- Describe important differences in structure between Archaea and Bacteria

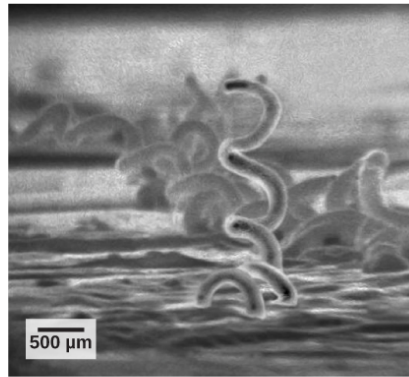
There are many differences between prokaryotic and eukaryotic cells. However, all cells have four common structures: the plasma membrane, which functions as a barrier for the cell and separates the cell from its environment; the cytoplasm, a jelly-like substance inside the cell; nucleic acids, the genetic material of the cell; and ribosomes, where protein synthesis takes place. Prokaryotes come in various shapes, but many fall into three categories: cocci (spherical), bacilli (rod-shaped), and spirilli (spiral-shaped) ([link](#)).



(a)



(b)

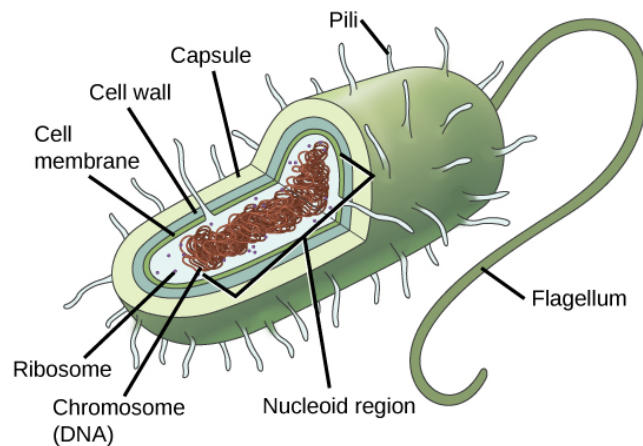


(c)

Prokaryotes fall into three basic categories based on their shape, visualized here using scanning electron microscopy: (a) cocci, or spherical (a pair is shown); (b) bacilli, or rod-shaped; and (c) spirilli, or spiral-shaped. (credit a: modification of work by Janice Haney Carr, Dr. Richard Facklam, CDC; credit c: modification of work by Dr. David Cox; scale-bar data from Matt Russell)

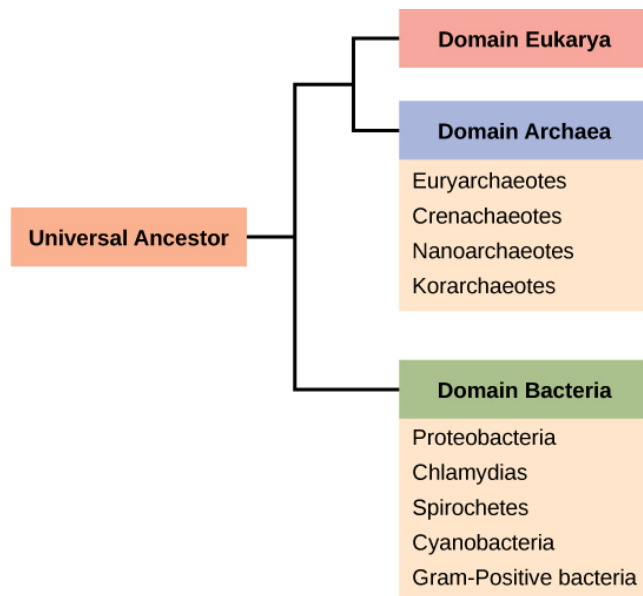
The Prokaryotic Cell

Recall that prokaryotes ([\[link\]](#)) are unicellular organisms that lack organelles or other internal membrane-bound structures. Therefore, they do not have a nucleus but instead generally have a single chromosome—a piece of circular, double-stranded DNA located in an area of the cell called the nucleoid. Most prokaryotes have a cell wall outside the plasma membrane.



The features of a typical prokaryotic cell are shown.

Recall that prokaryotes are divided into two different domains, Bacteria and Archaea, which together with Eukarya, comprise the three domains of life ([\[link\]](#)).

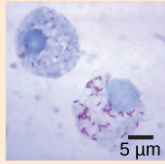
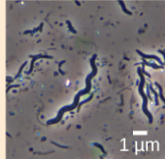
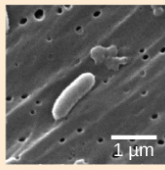
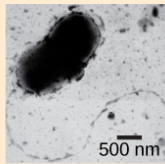
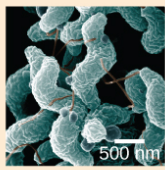


Bacteria and Archaea are both prokaryotes but differ enough to be placed in separate domains. An ancestor of modern Archaea is believed to have given rise to Eukarya, the third domain of life. Archaeal and bacterial phyla are shown; the evolutionary relationship between these phyla is still open to debate.

The composition of the cell wall differs significantly between the domains Bacteria and Archaea. The composition of their cell walls also differs from the eukaryotic cell walls found in plants (cellulose) or fungi and insects (chitin). The cell wall functions as a protective layer, and it is responsible for the organism's shape. Some bacteria have an outer **capsule** outside the cell wall. Other structures are present in some prokaryotic species, but not in others ([\[link\]](#)). For example, the capsule found in some species enables the organism to attach to surfaces, protects it from dehydration and attack by phagocytic cells, and makes pathogens more resistant to our immune responses. Some species also have flagella (singular, flagellum) used for

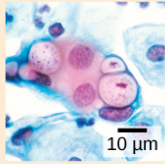
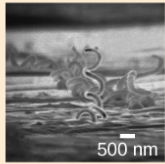
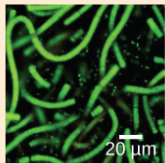
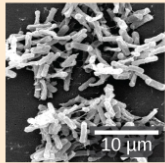
locomotion, and **pili** (singular, pilus) used for attachment to surfaces. Plasmids, which consist of extra-chromosomal DNA, are also present in many species of bacteria and archaea.

Characteristics of phyla of Bacteria are described in [\[link\]](#) and [\[link\]](#); Archaea are described in [\[link\]](#).

Bacteria of Phylum Proteobacteria		
Class	Representative organisms	Representative micrograph
Alpha Proteobacteria Some species are photoautotrophic but some are symbionts of plants and animals and others are pathogens. Eukaryotic mitochondria are thought to be derived from bacteria in this group.	<i>Rhizobium</i> Nitrogen-fixing endosymbiont associated with the roots of legumes <i>Rickettsia</i> Obligate intracellular parasite that causes typhus and Rocky Mountain Spotted Fever (but not ricketts, which is caused by Vitamin C deficiency)	 <i>Rickettsia rickettsia</i> , stained red, grow inside a host cell.
Beta Proteobacteria This group of bacteria is diverse. Some species play an important role in the nitrogen cycle.	<i>Nitrosomas</i> Species from this group oxidize ammonia into nitrite. <i>Spirillum minus</i> Causes rat-bite fever	 <i>Spirillum minus</i>
Gamma Proteobacteria Many are beneficial symbionts that populate the human gut, but others are familiar human pathogens. Some species from this subgroup oxidize sulfur compounds.	<i>Escherichia coli</i> Normally beneficial microbe of the human gut, but some strains cause disease <i>Salmonella</i> Certain strains cause food poisoning or typhoid fever <i>Yersinia pestis</i> Causative agent of Bubonic plague <i>Pseudomonas aeruginosa</i> Causes lung infections <i>Vibrio cholera</i> Causative agent of cholera <i>Chromatium</i> Sulfur-producing bacteria that oxidize sulfur, producing H ₂ S	 <i>Vibrio cholera</i>
Delta Proteobacteria Some species generate a spore-forming fruiting body in adverse conditions. Others reduce sulfate and sulfur.	<i>Myxobacteria</i> Generate spore-forming fruiting bodies in adverse conditions <i>Desulfovibrio vulgaris</i> Anaerobic, sulfate-reducing bacterium	 <i>Desulfovibrio vulgaris</i>
Epsilon Proteobacteria Many species inhabit the digestive tract of animals as symbionts or pathogens. Bacteria from this group have been found in deep-sea hydrothermal vents and cold seep habitats.	<i>Campylobacter</i> Causes blood poisoning and intestinal inflammation <i>Helicobacter pylori</i> Causes stomach ulcers	 <i>Campylobacter</i>

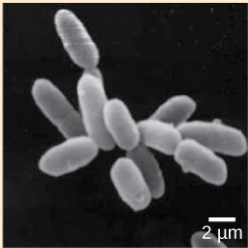
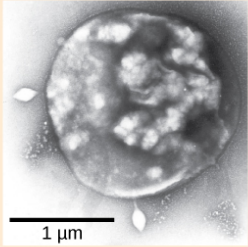
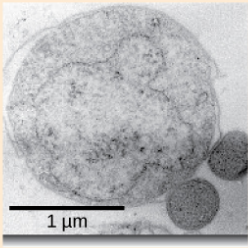
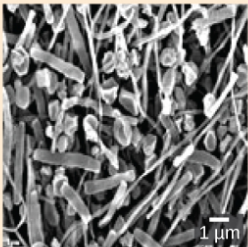
Phylum Proteobacteria is one of up to 52 bacteria phyla. Proteobacteria is further subdivided into five classes, Alpha through Epsilon. (credit “*Rickettsia rickettsia*”: modification of work by CDC; credit “*Spirillum minus*”: modification of work by Wolfram Adlassnig; credit “*Vibrio cholera*”: modification of work by Janice Haney Carr, CDC; credit “*Desulfovibrio*”

vulgaris”: modification of work by Graham Bradley; credit
 “Campylobacter”: modification of work by De Wood, Pooley,
 USDA, ARS, EMU; scale-bar data from Matt Russell)

Bacteria: Chlamydia, Spirochaetae, Cyanobacteria, and Gram-positive		
Phylum	Representative organisms	Representative micrograph
Chlamydias All members of this group are obligate intracellular parasites of animal cells. Cells walls lack peptidoglycan.	<i>Chlamydia trachomatis</i> Common sexually transmitted disease that can lead to blindness	 <p>10 μm</p> <p>In this pap smear, <i>Chlamydia trachomatis</i> appear as pink inclusions inside cells.</p>
Spirochetes Most members of this species, which has spiral-shaped cells, are free-living anaerobes, but some are pathogenic. Flagella run lengthwise in the periplasmic space between the inner and outer membrane.	<i>Treponema pallidum</i> Causative agent of syphilis <i>Borrelia burgdorferi</i> Causative agent of Lyme disease	 <p>500 nm</p> <p><i>Treponema pallidum</i></p>
Cyanobacteria Also known as blue-green algae, these bacteria obtain their energy through photosynthesis. They are ubiquitous, found in terrestrial, marine, and freshwater environments. Eukaryotic chloroplasts are thought to be derived from bacteria in this group.	<i>Prochlorococcus</i> Believed to be the most abundant photosynthetic organism on earth; responsible for generating half the world's oxygen	 <p>20 μm</p> <p><i>Phormidium</i></p>
Gram-positive Bacteria Soil-dwelling members of this subgroup decompose organic matter. Some species cause disease. They have a thick cell wall and lack an outer membrane.	<i>Bacillus anthracis</i> Causes anthrax <i>Clostridium botulinum</i> Causes Botulism <i>Clostridium difficile</i> Causes diarrhea during antibiotic therapy <i>Streptomyces</i> Many antibiotics, including streptomycin, are derived from these bacteria. <i>Mycoplasmas</i> These tiny bacteria, the smallest known, lack a cell wall. Some are free-living, and some are pathogenic.	 <p>10 μm</p> <p><i>Clostridium difficile</i></p>

Chlamydia, Spirochetes, Cyanobacteria, and Gram-positive bacteria are described in this table. Note that bacterial shape is not phylum-dependent; bacteria within a phylum may be cocci,

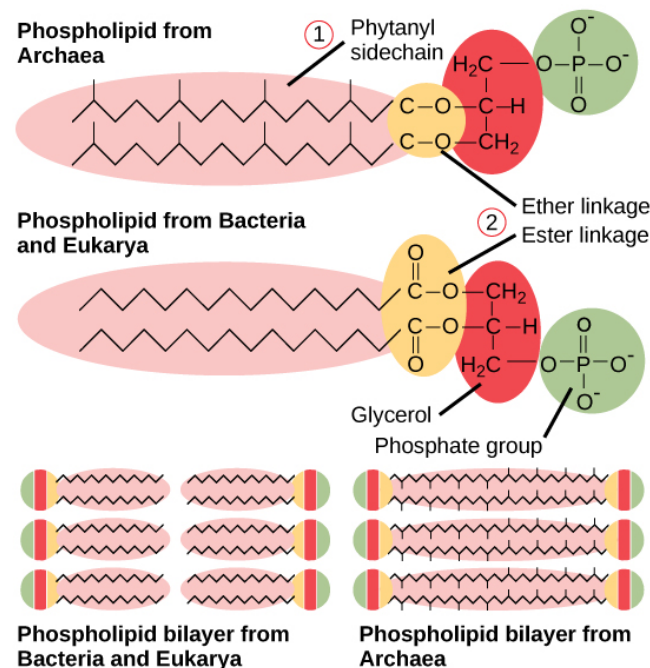
rod-shaped, or spiral. (credit “Chlamydia trachomatis”: modification of work by Dr. Lance Liotta Laboratory, NCI; credit “Treponema pallidum”: modification of work by Dr. David Cox, CDC; credit “Phormidium”: modification of work by USGS; credit “Clostridium difficile”: modification of work by Lois S. Wiggs, CDC; scale-bar data from Matt Russell)

Archaea		
Phylum	Representative organisms	Representative micrograph
Euryarchaeota This phylum includes methanogens, which produce methane as a metabolic waste product, and halobacteria, which live in an extreme saline environment.	<i>Methanogens</i> Methane production causes flatulence in humans and other animals. <i>Halobacteria</i> Large blooms of this salt-loving archaea appear reddish due to the presence of bacteriorhodopsin in the membrane. Bacteriorhodopsin is related to the retinal pigment rhodopsin.	 <p>2 μm</p> <p><i>Halobacterium</i> strain NRC-1</p>
Crenarchaeota Members of the ubiquitous phylum play an important role in the fixation of carbon. Many members of this group are sulfur-dependent extremophiles. Some are thermophilic or hyperthermophilic.	<i>Sulfolobus</i> Members of this genus grow in volcanic springs at temperatures between 75° and 80°C and at a pH between 2 and 3.	 <p>1 μm</p> <p><i>Sulfolobus</i> being infected by bacteriophage</p>
Nanoarchaeota This group currently contains only one species, <i>Nanoarchaeum equitans</i> .	<i>Nanoarchaeum equitans</i> This species was isolated from the bottom of the Atlantic Ocean and from a hydrothermal vent at Yellowstone National Park. It is an obligate symbiont with <i>Ignicoccus</i> , another species of archaea.	 <p>1 μm</p> <p><i>Nanoarchaeum equitans</i> (small dark spheres) are in contact with their larger host, <i>Ignicoccus</i>.</p>
Korarchaeota Members of this phylum, considered to be one of the most primitive forms of life, have only been found in the Obsidian Pool, a hot spring at Yellowstone National Park.	No members of this species have been cultivated.	 <p>1 μm</p> <p>This image shows a variety of korarchaeota species from the Obsidian Pool at Yellowstone National Park.</p>

Archaea are separated into four phyla: the Korarchaeota, Euryarchaeota, Crenarchaeota, and Nanoarchaeota. (credit “Halobacterium”: modification of work by NASA; credit “Nanoarchaeotum equitans”: modification of work by Karl O. Stetter; credit “korarchaeota”: modification of work by Office of Science of the U.S. Dept. of Energy; scale-bar data from Matt Russell)

The Plasma Membrane

The plasma membrane is a thin lipid bilayer (6 to 8 nanometers) that completely surrounds the cell and separates the inside from the outside. Its selectively permeable nature keeps ions, proteins, and other molecules within the cell and prevents them from diffusing into the extracellular environment, while other molecules may move through the membrane. Recall that the general structure of a cell membrane is a phospholipid bilayer composed of two layers of lipid molecules. In archaeal cell membranes, isoprene (phytanyl) chains linked to glycerol replace the fatty acids linked to glycerol in bacterial membranes. Some archaeal membranes are lipid monolayers instead of bilayers ([\[link\]](#)).



Archaeal phospholipids differ
from those found in Bacteria and

Eukarya in two ways. First, they have branched phytanyl sidechains instead of linear ones. Second, an ether bond instead of an ester bond connects the lipid to the glycerol.

The Cell Wall

The cytoplasm of prokaryotic cells has a high concentration of dissolved solutes. Therefore, the osmotic pressure within the cell is relatively high. The cell wall is a protective layer that surrounds some cells and gives them shape and rigidity. It is located outside the cell membrane and prevents osmotic lysis (bursting due to increasing volume). The chemical composition of the cell walls varies between archaea and bacteria, and also varies between bacterial species.

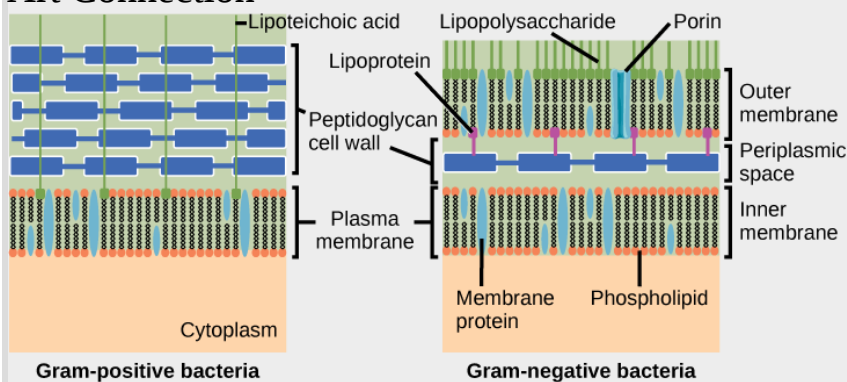
Bacterial cell walls contain **peptidoglycan**, composed of polysaccharide chains that are cross-linked by unusual peptides containing both L- and D-amino acids including D-glutamic acid and D-alanine. Proteins normally have only L-amino acids; as a consequence, many of our antibiotics work by mimicking D-amino acids and therefore have specific effects on bacterial cell wall development. There are more than 100 different forms of peptidoglycan. **S-layer** (surface layer) proteins are also present on the outside of cell walls of both archaea and bacteria.

Bacteria are divided into two major groups: **Gram positive** and **Gram negative**, based on their reaction to Gram staining. Note that all Gram-positive bacteria belong to one phylum; bacteria in the other phyla (Proteobacteria, Chlamydias, Spirochetes, Cyanobacteria, and others) are Gram-negative. The Gram staining method is named after its inventor, Danish scientist Hans Christian Gram (1853–1938). The different bacterial responses to the staining procedure are ultimately due to cell wall structure. Gram-positive organisms typically lack the outer membrane found in Gram-negative organisms ([\[link\]](#)). Up to 90 percent of the cell wall in Gram-

positive bacteria is composed of peptidoglycan, and most of the rest is composed of acidic substances called **teichoic acids**. Teichoic acids may be covalently linked to lipids in the plasma membrane to form lipoteichoic acids. Lipoteichoic acids anchor the cell wall to the cell membrane. Gram-negative bacteria have a relatively thin cell wall composed of a few layers of peptidoglycan (only 10 percent of the total cell wall), surrounded by an outer envelope containing lipopolysaccharides (LPS) and lipoproteins. This outer envelope is sometimes referred to as a second lipid bilayer. The chemistry of this outer envelope is very different, however, from that of the typical lipid bilayer that forms plasma membranes.

Note:

Art Connection



Bacteria are divided into two major groups: Gram positive and Gram negative. Both groups have a cell wall composed of peptidoglycan: in Gram-positive bacteria, the wall is thick, whereas in Gram-negative bacteria, the wall is thin. In Gram-negative bacteria, the cell wall is surrounded by an outer membrane that contains lipopolysaccharides and lipoproteins. Porins are proteins in this cell membrane that allow substances to pass through the outer membrane of Gram-negative bacteria. In Gram-positive bacteria, lipoteichoic acid anchors the cell wall to the cell membrane.

(credit: modification of work by
"Franciscop2"/Wikimedia Commons)

Which of the following statements is true?

- a. Gram-positive bacteria have a single cell wall anchored to the cell membrane by lipoteichoic acid.
- b. Porins allow entry of substances into both Gram-positive and Gram-negative bacteria.
- c. The cell wall of Gram-negative bacteria is thick, and the cell wall of Gram-positive bacteria is thin.
- d. Gram-negative bacteria have a cell wall made of peptidoglycan, whereas Gram-positive bacteria have a cell wall made of lipoteichoic acid.

Archaeal cell walls do not have peptidoglycan. There are four different types of Archaeal cell walls. One type is composed of **pseudopeptidoglycan**, which is similar to peptidoglycan in morphology but contains different sugars in the polysaccharide chain. The other three types of cell walls are composed of polysaccharides, glycoproteins, or pure protein.

Structural Differences and Similarities between Bacteria and Archaea		
Structural Characteristic	Bacteria	Archaea

Structural Differences and Similarities between Bacteria and Archaea		
Structural Characteristic	Bacteria	Archaea
Cell type	Prokaryotic	Prokaryotic
Cell morphology	Variable	Variable
Cell wall	Contains peptidoglycan	Does not contain peptidoglycan
Cell membrane type	Lipid bilayer	Lipid bilayer or lipid monolayer
Plasma membrane lipids	Fatty acids	Phytanyl groups

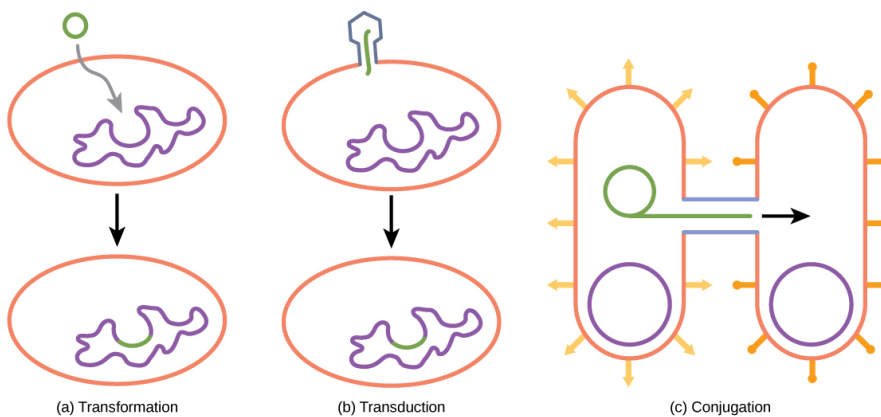
Reproduction

Reproduction in prokaryotes is asexual and usually takes place by binary fission. Recall that the DNA of a prokaryote exists as a single, circular chromosome. Prokaryotes do not undergo mitosis. Rather the chromosome is replicated and the two resulting copies separate from one another, due to the growth of the cell. The prokaryote, now enlarged, is pinched inward at its equator and the two resulting cells, which are clones, separate. Binary fission does not provide an opportunity for genetic recombination or genetic diversity, but prokaryotes can share genes by three other mechanisms.

In **transformation**, the prokaryote takes in DNA found in its environment that is shed by other prokaryotes. If a nonpathogenic bacterium takes up DNA for a toxin gene from a pathogen and incorporates the new DNA into its own chromosome, it too may become pathogenic. In **transduction**, bacteriophages, the viruses that infect bacteria, sometimes also move short pieces of chromosomal DNA from one bacterium to another. Transduction

results in a recombinant organism. Archaea are not affected by bacteriophages but instead have their own viruses that translocate genetic material from one individual to another. In **conjugation**, DNA is transferred from one prokaryote to another by means of a pilus, which brings the organisms into contact with one another. The DNA transferred can be in the form of a plasmid or as a hybrid, containing both plasmid and chromosomal DNA. These three processes of DNA exchange are shown in [\[link\]](#).

Reproduction can be very rapid: a few minutes for some species. This short generation time coupled with mechanisms of genetic recombination and high rates of mutation result in the rapid evolution of prokaryotes, allowing them to respond to environmental changes (such as the introduction of an antibiotic) very quickly.



Besides binary fission, there are three other mechanisms by which prokaryotes can exchange DNA. In (a) transformation, the cell takes up prokaryotic DNA directly from the environment. The DNA may remain separate as plasmid DNA or be incorporated into the host genome. In (b) transduction, a bacteriophage injects DNA into the cell that contains a small fragment of DNA from a different prokaryote. In (c) conjugation, DNA is transferred from one cell to another via a mating bridge that connects the two cells after the

sex pilus draws the two bacteria close enough to form the bridge.

Note:

Evolution Connection

The Evolution of Prokaryotes

How do scientists answer questions about the evolution of prokaryotes? Unlike with animals, artifacts in the fossil record of prokaryotes offer very little information. Fossils of ancient prokaryotes look like tiny bubbles in rock. Some scientists turn to genetics and to the principle of the molecular clock, which holds that the more recently two species have diverged, the more similar their genes (and thus proteins) will be. Conversely, species that diverged long ago will have more genes that are dissimilar.

Scientists at the NASA Astrobiology Institute and at the European Molecular Biology Laboratory collaborated to analyze the molecular evolution of 32 specific proteins common to 72 species of prokaryotes.

[\[footnote\]](#) The model they derived from their data indicates that three important groups of bacteria—Actinobacteria, *Deinococcus*, and Cyanobacteria (which the authors call *Terrabacteria*)—were the first to colonize land. (Recall that *Deinococcus* is a genus of prokaryote—a bacterium—that is highly resistant to ionizing radiation.) Cyanobacteria are photosynthesizers, while Actinobacteria are a group of very common bacteria that include species important in decomposition of organic wastes. Battistuzzi, FU, Feijao, A, and Hedges, SB. A genomic timescale of prokaryote evolution: Insights into the origin of methanogenesis, phototrophy, and the colonization of land. *BioMed Central: Evolutionary Biology* 4 (2004): 44, doi:10.1186/1471-2148-4-44.

The timelines of divergence suggest that bacteria (members of the domain Bacteria) diverged from common ancestral species between 2.5 and 3.2 billion years ago, whereas archaea diverged earlier: between 3.1 and 4.1 billion years ago. Eukarya later diverged off the Archaeal line. The work further suggests that stromatolites that formed prior to the advent of cyanobacteria (about 2.6 billion years ago) photosynthesized in an anoxic environment and that because of the modifications of the Terrabacteria for

land (resistance to drying and the possession of compounds that protect the organism from excess light), photosynthesis using oxygen may be closely linked to adaptations to survive on land.

Section Summary

Prokaryotes (domains Archaea and Bacteria) are single-celled organisms lacking a nucleus. They have a single piece of circular DNA in the nucleoid area of the cell. Most prokaryotes have a cell wall that lies outside the boundary of the plasma membrane. Some prokaryotes may have additional structures such as a capsule, flagella, and pili. Bacteria and Archaea differ in the lipid composition of their cell membranes and the characteristics of the cell wall. In archaeal membranes, phytanyl units, rather than fatty acids, are linked to glycerol. Some archaeal membranes are lipid monolayers instead of bilayers.

The cell wall is located outside the cell membrane and prevents osmotic lysis. The chemical composition of cell walls varies between species. Bacterial cell walls contain peptidoglycan. Archaeal cell walls do not have peptidoglycan, but they may have pseudopeptidoglycan, polysaccharides, glycoproteins, or protein-based cell walls. Bacteria can be divided into two major groups: Gram positive and Gram negative, based on the Gram stain reaction. Gram-positive organisms have a thick cell wall, together with teichoic acids. Gram-negative organisms have a thin cell wall and an outer envelope containing lipopolysaccharides and lipoproteins.

Art Connections

Exercise:

Problem: [\[link\]](#) Which of the following statements is true?

- a. Gram-positive bacteria have a single cell wall anchored to the cell membrane by lipoteichoic acid.

- b. Porins allow entry of substances into both Gram-positive and Gram-negative bacteria.
 - c. The cell wall of Gram-negative bacteria is thick, and the cell wall of Gram-positive bacteria is thin.
 - d. Gram-negative bacteria have a cell wall made of peptidoglycan, whereas Gram-positive bacteria have a cell wall made of lipoteichoic acid.
-

Solution:

[\[link\]](#) A

Review Questions

Exercise:

Problem:

The presence of a membrane-enclosed nucleus is a characteristic of _____.

- a. prokaryotic cells
 - b. eukaryotic cells
 - c. all cells
 - d. viruses
-

Solution:

B

Exercise:

Problem: Which of the following consist of prokaryotic cells?

- a. bacteria and fungi
- b. archaea and fungi

- c. protists and animals
- d. bacteria and archaea

Solution:

D

Exercise:

Problem: The cell wall is _____.

- a. interior to the cell membrane
- b. exterior to the cell membrane
- c. a part of the cell membrane
- d. interior or exterior, depending on the particular cell

Solution:

B

Exercise:

Problem:

Organisms most likely to be found in extreme environments are _____.

- a. fungi
- b. bacteria
- c. viruses
- d. archaea

Solution:

B

Exercise:

Problem:

Prokaryotes stain as Gram-positive or Gram-negative because of differences in the cell _____.

- a. wall
- b. cytoplasm
- c. nucleus
- d. chromosome

Solution:

A

Exercise:**Problem:**

Pseudopeptidoglycan is a characteristic of the walls of _____.

- a. eukaryotic cells
- b. bacterial prokaryotic cells
- c. archaean prokaryotic cells
- d. bacterial and archaean prokaryotic cells

Solution:

C

Exercise:**Problem:**

The lipopolysaccharide layer (LPS) is a characteristic of the wall of _____.

- a. archaean cells
- b. Gram-negative bacteria

- c. bacterial prokaryotic cells
- d. eukaryotic cells

Solution:

B

Free Response

Exercise:

Problem: Mention three differences between bacteria and archaea.

Solution:

Responses will vary. A possible answer is: Bacteria contain peptidoglycan in the cell wall; archaea do not. The cell membrane in bacteria is a lipid bilayer; in archaea, it can be a lipid bilayer or a monolayer. Bacteria contain fatty acids on the cell membrane, whereas archaea contain phytanyl.

Exercise:

Problem:

Explain the statement that both types, bacteria and archaea, have the same basic structures, but built from different chemical components.

Solution:

Both bacteria and archaea have cell membranes and they both contain a hydrophobic portion. In the case of bacteria, it is a fatty acid; in the case of archaea, it is a hydrocarbon (phytanyl). Both bacteria and archaea have a cell wall that protects them. In the case of bacteria, it is composed of peptidoglycan, whereas in the case of archaea, it is pseudopeptidoglycan, polysaccharides, glycoproteins, or pure protein. Bacterial and archaeal flagella also differ in their chemical structure.

Glossary

capsule

external structure that enables a prokaryote to attach to surfaces and protects it from dehydration

conjugation

process by which prokaryotes move DNA from one individual to another using a pilus

Gram negative

bacterium whose cell wall contains little peptidoglycan but has an outer membrane

Gram positive

bacterium that contains mainly peptidoglycan in its cell walls

peptidoglycan

material composed of polysaccharide chains cross-linked to unusual peptides

pilus

surface appendage of some prokaryotes used for attachment to surfaces including other prokaryotes

pseudopeptidoglycan

component of archaea cell walls that is similar to peptidoglycan in morphology but contains different sugars

S-layer

surface-layer protein present on the outside of cell walls of archaea and bacteria

teichoic acid

polymer associated with the cell wall of Gram-positive bacteria

transduction

process by which a bacteriophage moves DNA from one prokaryote to another

transformation

process by which a prokaryote takes in DNA found in its environment that is shed by other prokaryotes

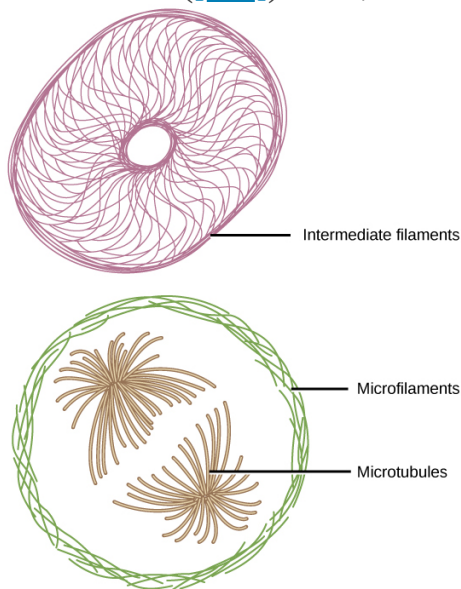
Bis2A 10.3 The Cytoskeleton

By the end of this section, you will be able to:

- Describe the cytoskeleton
- Compare the roles of microfilaments, intermediate filaments, and microtubules
- Compare and contrast cilia and flagella
- Summarize the differences among the components of prokaryotic cells, animal cells, and plant cells

If you were to remove all the organelles from a cell, would the plasma membrane and the cytoplasm be the only components left? No. Within the cytoplasm, there would still be ions and organic molecules, plus a network of protein fibers that help maintain the shape of the cell, secure some organelles in specific positions, allow cytoplasm and vesicles to move within the cell, and enable cells within multicellular organisms to move.

Collectively, this network of protein fibers is known as the **cytoskeleton**. There are three types of fibers within the cytoskeleton: microfilaments, intermediate filaments, and microtubules ([\[link\]](#)). Here, we will examine each.



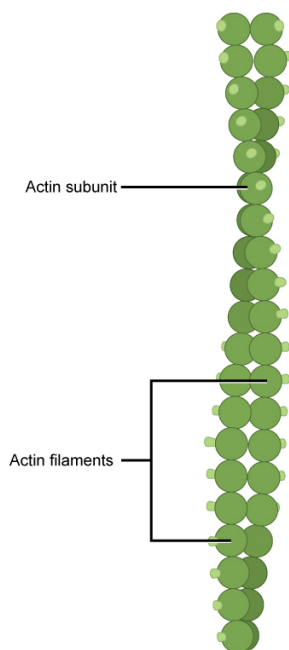
Microfilaments thicken the cortex around the inner edge of a cell; like rubber bands, they resist tension.

Microtubules are found in the interior of the cell where they maintain cell shape by resisting compressive forces.

Intermediate filaments are found throughout the cell and hold organelles in place.

Microfilaments

Of the three types of protein fibers in the cytoskeleton, **microfilaments** are the narrowest. They function in cellular movement, have a diameter of about 7 nm, and are made of two intertwined strands of a globular protein called actin ([link](#)). For this reason, microfilaments are also known as actin filaments.



Microfilaments are made of two intertwined strands of actin.

Actin is powered by ATP to assemble its filamentous form, which serves as a track for the movement of a motor protein called myosin. This enables actin to engage in cellular events requiring motion, such as cell division in animal cells and cytoplasmic streaming, which is the circular movement of the cell cytoplasm in plant cells. Actin and myosin are plentiful in muscle cells. When your actin and myosin filaments slide past each other, your muscles contract.

Microfilaments also provide some rigidity and shape to the cell. They can depolymerize (disassemble) and reform quickly, thus enabling a cell to change its shape and move.

White blood cells (your body's infection-fighting cells) make good use of this ability. They can move to the site of an infection and phagocytize the pathogen.

Note:

Link to Learning



To see an example of a white blood cell in action, click [here](#) and watch a short time-lapse video of the cell capturing two bacteria. It engulfs one and then moves on to the other.

Intermediate Filaments

Intermediate filaments are made of several strands of fibrous proteins that are wound together ([link](#)). These elements of the cytoskeleton get their name from the fact that their diameter, 8 to 10 nm, is between those of microfilaments and microtubules.



Intermediate filaments consist of several intertwined strands of fibrous proteins.

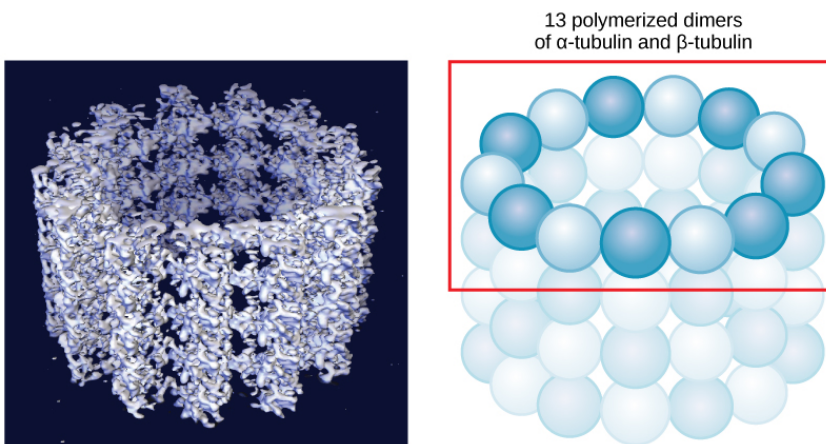
Intermediate filaments have no role in cell movement. Their function is purely structural. They bear tension, thus maintaining the shape of the cell, and anchor the nucleus and other organelles in place. [link](#) shows how intermediate filaments create a supportive scaffolding inside the cell.

The intermediate filaments are the most diverse group of cytoskeletal elements. Several types of fibrous proteins are found in the intermediate filaments. You are probably most

familiar with keratin, the fibrous protein that strengthens your hair, nails, and the epidermis of the skin.

Microtubules

As their name implies, microtubules are small hollow tubes. The walls of the microtubule are made of polymerized dimers of α -tubulin and β -tubulin, two globular proteins ([\[link\]](#)). With a diameter of about 25 nm, **microtubules** are the widest components of the cytoskeleton. They help the cell resist compression, provide a track along which vesicles move through the cell, and pull replicated chromosomes to opposite ends of a dividing cell. Like microfilaments, microtubules can dissolve and reform quickly.



Microtubules are hollow. Their walls consist of 13 polymerized dimers of α -tubulin and β -tubulin (right image). The left image shows the molecular structure of the tube.

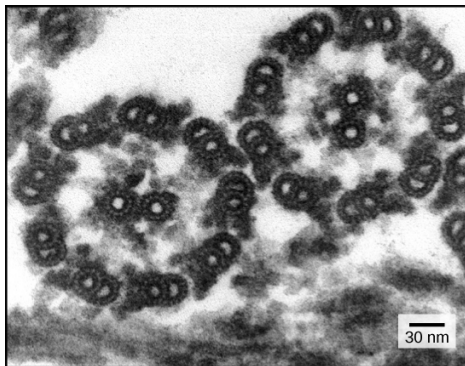
Microtubules are also the structural elements of flagella, cilia, and centrioles (the latter are the two perpendicular bodies of the centrosome). In fact, in animal cells, the centrosome is the microtubule-organizing center. In eukaryotic cells, flagella and cilia are quite different structurally from their counterparts in prokaryotes, as discussed below.

Flagella and Cilia

To refresh your memory, **flagella** (singular = flagellum) are long, hair-like structures that extend from the plasma membrane and are used to move an entire cell (for example,

sperm, *Euglena*). When present, the cell has just one flagellum or a few flagella. When **cilia** (singular = cilium) are present, however, many of them extend along the entire surface of the plasma membrane. They are short, hair-like structures that are used to move entire cells (such as paramecia) or substances along the outer surface of the cell (for example, the cilia of cells lining the Fallopian tubes that move the ovum toward the uterus, or cilia lining the cells of the respiratory tract that trap particulate matter and move it toward your nostrils.)

Despite their differences in length and number, flagella and cilia share a common structural arrangement of microtubules called a “9 + 2 array.” This is an appropriate name because a single flagellum or cilium is made of a ring of nine microtubule doublets, surrounding a single microtubule doublet in the center ([link](#)).



This transmission electron micrograph of two flagella shows the 9 + 2 array of microtubules: nine microtubule doublets surround a single microtubule doublet. (credit: modification of work by Dartmouth Electron Microscope Facility, Dartmouth College; scale-bar data from Matt Russell)

You have now completed a broad survey of the components of prokaryotic and eukaryotic cells. For a summary of cellular components in prokaryotic and eukaryotic cells, see [link](#).

Components of Prokaryotic and Eukaryotic Cells				
Cell Component	Function	Present in Prokaryotes?	Present in Animal Cells?	Present in Plant Cells?
Plasma membrane	Separates cell from external environment; controls passage of organic molecules, ions, water, oxygen, and wastes into and out of cell	Yes	Yes	Yes
Cytoplasm	Provides turgor pressure to plant cells as fluid inside the central vacuole; site of many metabolic reactions; medium in which organelles are found	Yes	Yes	Yes
Nucleolus	Darkened area within the nucleus where ribosomal subunits are synthesized.	No	Yes	Yes
Nucleus	Cell organelle that houses DNA and directs synthesis of ribosomes and proteins	No	Yes	Yes
Ribosomes	Protein synthesis	Yes	Yes	Yes

Components of Prokaryotic and Eukaryotic Cells				
Cell Component	Function	Present in Prokaryotes?	Present in Animal Cells?	Present in Plant Cells?
Mitochondria	ATP production/cellular respiration	No	Yes	Yes
Peroxisomes	Oxidizes and thus breaks down fatty acids and amino acids, and detoxifies poisons	No	Yes	Yes
Vesicles and vacuoles	Storage and transport; digestive function in plant cells	No	Yes	Yes
Centrosome	Unspecified role in cell division in animal cells; source of microtubules in animal cells	No	Yes	No
Lysosomes	Digestion of macromolecules; recycling of worn-out organelles	No	Yes	No
Cell wall	Protection, structural support and maintenance of cell shape	Yes, primarily peptidoglycan	No	Yes, primarily cellulose
Chloroplasts	Photosynthesis	No	No	Yes

Components of Prokaryotic and Eukaryotic Cells				
Cell Component	Function	Present in Prokaryotes?	Present in Animal Cells?	Present in Plant Cells?
Endoplasmic reticulum	Modifies proteins and synthesizes lipids	No	Yes	Yes
Golgi apparatus	Modifies, sorts, tags, packages, and distributes lipids and proteins	No	Yes	Yes
Cytoskeleton	Maintains cell's shape, secures organelles in specific positions, allows cytoplasm and vesicles to move within cell, and enables unicellular organisms to move independently	Yes	Yes	Yes
Flagella	Cellular locomotion	Some	Some	No, except for some plant sperm cells.
Cilia	Cellular locomotion, movement of particles along extracellular surface of plasma membrane, and filtration	Some	Some	No

Section Summary

The cytoskeleton has three different types of protein elements. From narrowest to widest, they are the microfilaments (actin filaments), intermediate filaments, and microtubules. Microfilaments are often associated with myosin. They provide rigidity and shape to the cell and facilitate cellular movements. Intermediate filaments bear tension and anchor the nucleus and other organelles in place. Microtubules help the cell resist compression, serve as tracks for motor proteins that move vesicles through the cell, and pull replicated chromosomes to opposite ends of a dividing cell. They are also the structural element of centrioles, flagella, and cilia.

Review Questions

Exercise:

Problem:

Which of the following have the ability to disassemble and reform quickly?

- a. microfilaments and intermediate filaments
- b. microfilaments and microtubules
- c. intermediate filaments and microtubules
- d. only intermediate filaments

Solution:

B

Exercise:

Problem: Which of the following do not play a role in intracellular movement?

- a. microfilaments and intermediate filaments
- b. microfilaments and microtubules
- c. intermediate filaments and microtubules
- d. only intermediate filaments

Solution:

D

Free Response

Exercise:**Problem:**

What are the similarities and differences between the structures of centrioles and flagella?

Solution:

Centrioles and flagella are alike in that they are made up of microtubules. In centrioles, two rings of nine microtubule “triplets” are arranged at right angles to one another. This arrangement does not occur in flagella.

Exercise:

Problem:How do cilia and flagella differ?

Solution:

Cilia and flagella are alike in that they are made up of microtubules. Cilia are short, hair-like structures that exist in large numbers and usually cover the entire surface of the plasma membrane. Flagella, in contrast, are long, hair-like structures; when flagella are present, a cell has just one or two.

Glossary**cilium**

(plural = cilia) short, hair-like structure that extends from the plasma membrane in large numbers and is used to move an entire cell or move substances along the outer surface of the cell

cytoskeleton

network of protein fibers that collectively maintain the shape of the cell, secure some organelles in specific positions, allow cytoplasm and vesicles to move within the cell, and enable unicellular organisms to move independently

flagellum

(plural = flagella) long, hair-like structure that extends from the plasma membrane and is used to move the cell

intermediate filament

cytoskeletal component, composed of several intertwined strands of fibrous protein, that bears tension, supports cell-cell junctions, and anchors cells to extracellular structures

microfilament

narrowest element of the cytoskeleton system; it provides rigidity and shape to the cell and enables cellular movements

microtubule

widest element of the cytoskeleton system; it helps the cell resist compression, provides a track along which vesicles move through the cell, pulls replicated chromosomes to opposite ends of a dividing cell, and is the structural element of centrioles, flagella, and cilia

Bis2A 10.4 The Endomembrane System and Proteins

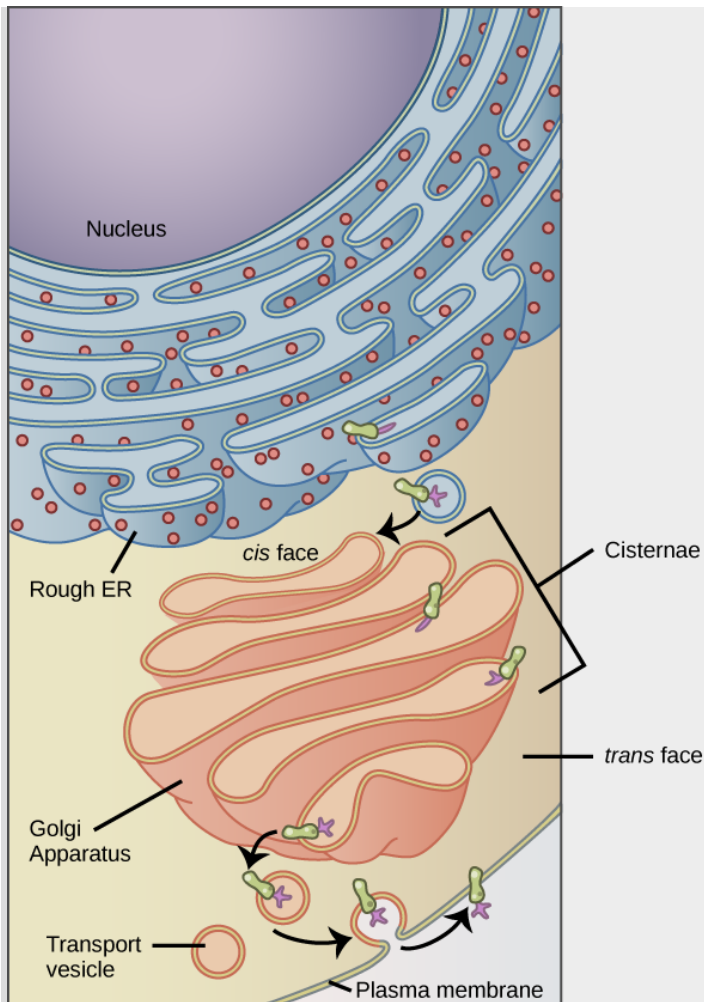
By the end of this section, you will be able to:

- List the components of the endomembrane system
- Recognize the relationship between the endomembrane system and its functions

The endomembrane system (endo = “within”) is a group of membranes and organelles ([\[link\]](#)) in eukaryotic cells that works together to modify, package, and transport lipids and proteins. It includes the nuclear envelope, lysosomes, and vesicles, which we’ve already mentioned, and the endoplasmic reticulum and Golgi apparatus, which we will cover shortly. Although not technically *within* the cell, the plasma membrane is included in the endomembrane system because, as you will see, it interacts with the other endomembranous organelles. The endomembrane system does not include the membranes of either mitochondria or chloroplasts.

Note:

Art Connection



"Membrane and secretory proteins are synthesized in the rough endoplasmic reticulum (RER). The RER also sometimes modifies proteins. In this illustration, a (green) integral membrane protein in the ER is modified by attachment of a (purple) carbohydrate. Vesicles with the integral protein bud from the ER and fuse with the cis face of the Golgi apparatus. As the protein passes along the Golgi's cisternae, it is further modified by the addition of more carbohydrates. After its synthesis is

complete, it exits as integral membrane protein of the vesicle that bud from the Golgi's **trans** face and when the vesicle fuses with the cell membrane the protein becomes integral portion of that cell membrane.
(credit: modification of work by Magnus Manske)

If a peripheral membrane protein were synthesized in the lumen (inside) of the ER, would it end up on the inside or outside of the plasma membrane?

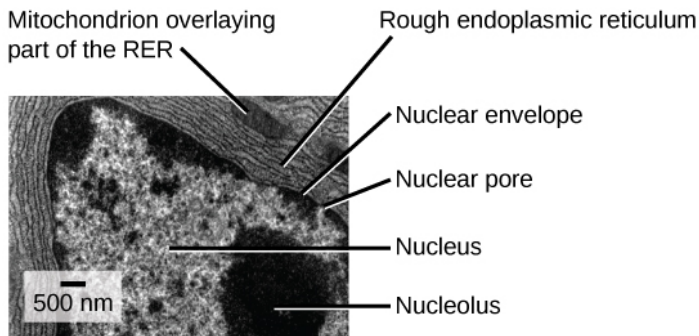
The Endoplasmic Reticulum

The **endoplasmic reticulum (ER)** ([\[link\]](#)) is a series of interconnected membranous sacs and tubules that collectively modifies proteins and synthesizes lipids. However, these two functions are performed in separate areas of the ER: the rough ER and the smooth ER, respectively.

The hollow portion of the ER tubules is called the lumen or cisternal space. The membrane of the ER, which is a phospholipid bilayer embedded with proteins, is continuous with the nuclear envelope.

Rough ER

The **rough endoplasmic reticulum (RER)** is so named because the ribosomes attached to its cytoplasmic surface give it a studded appearance when viewed through an electron microscope ([\[link\]](#)).



This transmission electron micrograph shows the rough endoplasmic reticulum and other organelles in a pancreatic cell. (credit: modification of work by Louisa Howard)

Ribosomes transfer their newly synthesized proteins into the lumen of the RER where they undergo structural modifications, such as folding or the acquisition of side chains. These modified proteins will be incorporated into cellular membranes—the membrane of the ER or those of other organelles—or secreted from the cell (such as protein hormones, enzymes). The RER also makes phospholipids for cellular membranes.

If the phospholipids or modified proteins are not destined to stay in the RER, they will reach their destinations via transport vesicles that bud from the RER's membrane ([\[link\]](#)).

Since the RER is engaged in modifying proteins (such as enzymes, for example) that will be secreted from the cell, you would be correct in assuming that the RER is abundant in cells that secrete proteins. This is the case with cells of the liver, for example.

Smooth ER

The **smooth endoplasmic reticulum (SER)** is continuous with the RER but has few or no ribosomes on its cytoplasmic surface ([\[link\]](#)). Functions

of the SER include synthesis of carbohydrates, lipids, and steroid hormones; detoxification of medications and poisons; and storage of calcium ions.

In muscle cells, a specialized SER called the sarcoplasmic reticulum is responsible for storage of the calcium ions that are needed to trigger the coordinated contractions of the muscle cells.

Note:

Link to Learning



You can watch an excellent animation of the endomembrane system [here](#). At the end of the animation, there is a short self-assessment.

Note:

Career Connection

Cardiologist

Heart disease is the leading cause of death in the United States. This is primarily due to our sedentary lifestyle and our high trans-fat diets.

Heart failure is just one of many disabling heart conditions. Heart failure does not mean that the heart has stopped working. Rather, it means that the heart can't pump with sufficient force to transport oxygenated blood to all the vital organs. Left untreated, heart failure can lead to kidney failure and failure of other organs.

The wall of the heart is composed of cardiac muscle tissue. Heart failure occurs when the endoplasmic reticula of cardiac muscle cells do not

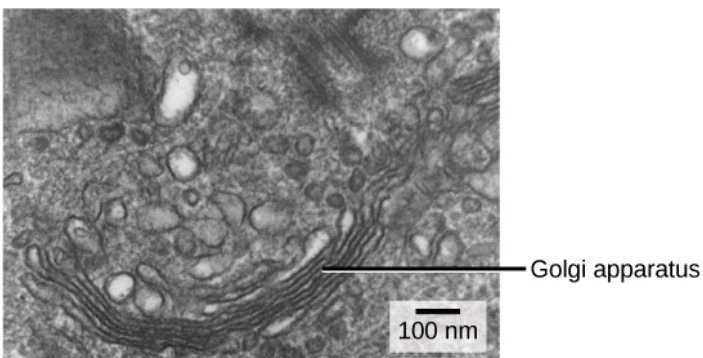
function properly. As a result, an insufficient number of calcium ions are available to trigger a sufficient contractile force.

Cardiologists (cardi- = “heart”; -ologist = “one who studies”) are doctors who specialize in treating heart diseases, including heart failure.

Cardiologists can make a diagnosis of heart failure via physical examination, results from an electrocardiogram (ECG, a test that measures the electrical activity of the heart), a chest X-ray to see whether the heart is enlarged, and other tests. If heart failure is diagnosed, the cardiologist will typically prescribe appropriate medications and recommend a reduction in table salt intake and a supervised exercise program.

The Golgi Apparatus

We have already mentioned that vesicles can bud from the ER and transport their contents elsewhere, but where do the vesicles go? Before reaching their final destination, the lipids or proteins within the transport vesicles still need to be sorted, packaged, and tagged so that they wind up in the right place. Sorting, tagging, packaging, and distribution of lipids and proteins takes place in the **Golgi apparatus** (also called the Golgi body), a series of flattened membranes ([\[link\]](#)).



The Golgi apparatus in this white blood cell is visible as a stack of semicircular, flattened rings in the lower portion of the image. Several

vesicles can be seen near the Golgi apparatus. (credit: modification of work by Louisa Howard)

The receiving side of the Golgi apparatus is called the *cis* face. The opposite side is called the *trans* face. The transport vesicles that formed from the ER travel to the *cis* face, fuse with it, and empty their contents into the lumen of the Golgi apparatus. As the proteins and lipids travel through the Golgi, they undergo further modifications that allow them to be sorted. The most frequent modification is the addition of short chains of sugar molecules. These newly modified proteins and lipids are then tagged with phosphate groups or other small molecules so that they can be routed to their proper destinations.

Finally, the modified and tagged proteins are packaged into secretory vesicles that bud from the *trans* face of the Golgi. While some of these vesicles deposit their contents into other parts of the cell where they will be used, other secretory vesicles fuse with the plasma membrane and release their contents outside the cell.

In another example of form following function, cells that engage in a great deal of secretory activity (such as cells of the salivary glands that secrete digestive enzymes or cells of the immune system that secrete antibodies) have an abundance of Golgi.

In plant cells, the Golgi apparatus has the additional role of synthesizing polysaccharides, some of which are incorporated into the cell wall and some of which are used in other parts of the cell.

Note:**Career Connection****Geneticist**

Many diseases arise from genetic mutations that prevent the synthesis of critical proteins. One such disease is Lowe disease (also called

oculocerebrorenal syndrome, because it affects the eyes, brain, and kidneys). In Lowe disease, there is a deficiency in an enzyme localized to the Golgi apparatus. Children with Lowe disease are born with cataracts, typically develop kidney disease after the first year of life, and may have impaired mental abilities.

Lowe disease is a genetic disease caused by a mutation on the X chromosome. The X chromosome is one of the two human sex chromosomes, as these chromosomes determine a person's sex. Females possess two X chromosomes while males possess one X and one Y chromosome. In females, the genes on only one of the two X chromosomes are expressed. Therefore, females who carry the Lowe disease gene on one of their X chromosomes have a 50/50 chance of having the disease.

However, males only have one X chromosome and the genes on this chromosome are always expressed. Therefore, males will always have Lowe disease if their X chromosome carries the Lowe disease gene. The location of the mutated gene, as well as the locations of many other mutations that cause genetic diseases, has now been identified. Through prenatal testing, a woman can find out if the fetus she is carrying may be afflicted with one of several genetic diseases.

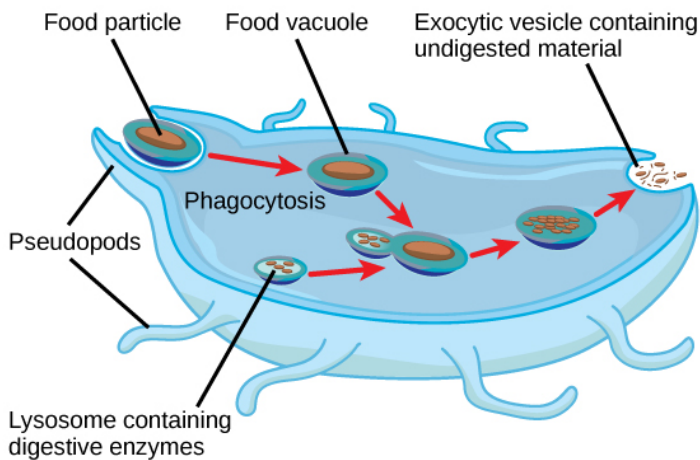
Geneticists analyze the results of prenatal genetic tests and may counsel pregnant women on available options. They may also conduct genetic research that leads to new drugs or foods, or perform DNA analyses that are used in forensic investigations.

Lysosomes

In addition to their role as the digestive component and organelle-recycling facility of animal cells, lysosomes are considered to be parts of the endomembrane system. Lysosomes also use their hydrolytic enzymes to destroy pathogens (disease-causing organisms) that might enter the cell. A good example of this occurs in a group of white blood cells called macrophages, which are part of your body's immune system. In a process known as phagocytosis or endocytosis, a section of the plasma membrane of the macrophage invaginates (folds in) and engulfs a pathogen. The invaginated section, with the pathogen inside, then pinches itself off from

the plasma membrane and becomes a vesicle. The vesicle fuses with a lysosome. The lysosome's hydrolytic enzymes then destroy the pathogen ([link](#)).

Phagocytosis



A macrophage has engulfed (phagocytized) a potentially pathogenic bacterium and then fuses with a lysosomes within the cell to destroy the pathogen. Other organelles are present in the cell but for simplicity are not shown.

Section Summary

The endomembrane system includes the nuclear envelope, lysosomes, vesicles, the ER, and Golgi apparatus, as well as the plasma membrane. These cellular components work together to modify, package, tag, and transport proteins and lipids that form the membranes.

The RER modifies proteins and synthesizes phospholipids used in cell membranes. The SER synthesizes carbohydrates, lipids, and steroid

hormones; engages in the detoxification of medications and poisons; and stores calcium ions. Sorting, tagging, packaging, and distribution of lipids and proteins take place in the Golgi apparatus. Lysosomes are created by the budding of the membranes of the RER and Golgi. Lysosomes digest macromolecules, recycle worn-out organelles, and destroy pathogens.

Art Connections

Exercise:

Problem:

[\[link\]](#) If a peripheral membrane protein were synthesized in the lumen (inside) of the ER, would it end up on the inside or outside of the plasma membrane?

Solution:

[\[link\]](#) It would end up on the outside. After the vesicle passes through the Golgi apparatus and fuses with the plasma membrane, it turns inside out.

Review Questions

Exercise:

Problem:

Which of the following is not a component of the endomembrane system?

- a. mitochondrion
 - b. Golgi apparatus
 - c. endoplasmic reticulum
 - d. lysosome
-

Solution:

A

Exercise:

Problem:

The process by which a cell engulfs a foreign particle is known as:

- a. endosymbiosis
- b. phagocytosis
- c. hydrolysis
- d. membrane synthesis

Solution:

B

Exercise:

Problem:

Which of the following is most likely to have the greatest concentration of smooth endoplasmic reticulum?

- a. a cell that secretes enzymes
- b. a cell that destroys pathogens
- c. a cell that makes steroid hormones
- d. a cell that engages in photosynthesis

Solution:

C

Exercise:

Problem:

Which of the following sequences correctly lists in order the steps involved in the incorporation of a proteinaceous molecule within a cell?

- a. synthesis of the protein on the ribosome; modification in the Golgi apparatus; packaging in the endoplasmic reticulum; tagging in the vesicle
 - b. synthesis of the protein on the lysosome; tagging in the Golgi; packaging in the vesicle; distribution in the endoplasmic reticulum
 - c. synthesis of the protein on the ribosome; modification in the endoplasmic reticulum; tagging in the Golgi; distribution via the vesicle
 - d. synthesis of the protein on the lysosome; packaging in the vesicle; distribution via the Golgi; tagging in the endoplasmic reticulum
-

Solution:

C

Free Response

Exercise:

Problem:

In the context of cell biology, what do we mean by form follows function? What are at least two examples of this concept?

Solution:

“Form follows function” refers to the idea that the function of a body part dictates the form of that body part. As an example, compare your arm to a bat’s wing. While the bones of the two correspond, the parts serve different functions in each organism and their forms have adapted to follow that function.

Exercise:

Problem:

In your opinion, is the nuclear membrane part of the endomembrane system? Why or why not? Defend your answer.

Solution:

Since the external surface of the nuclear membrane is continuous with the rough endoplasmic reticulum, which is part of the endomembrane system, then it is correct to say that it is part of the system.

Glossary

endomembrane system

group of organelles and membranes in eukaryotic cells that work together modifying, packaging, and transporting lipids and proteins

endoplasmic reticulum (ER)

series of interconnected membranous structures within eukaryotic cells that collectively modify proteins and synthesize lipids

Golgi apparatus

eukaryotic organelle made up of a series of stacked membranes that sorts, tags, and packages lipids and proteins for distribution

rough endoplasmic reticulum (RER)

region of the endoplasmic reticulum that is studded with ribosomes and engages in protein modification and phospholipid synthesis

smooth endoplasmic reticulum (SER)

region of the endoplasmic reticulum that has few or no ribosomes on its cytoplasmic surface and synthesizes carbohydrates, lipids, and steroid hormones; detoxifies certain chemicals (like pesticides, preservatives, medications, and environmental pollutants), and stores calcium ions

Bis2A 10.5 Eukaryotic Origins

By the end of this section, you will be able to:

- List the unifying characteristics of eukaryotes
- Describe what scientists know about the origins of eukaryotes based on the last common ancestor
- Explain endosymbiotic theory

Living things fall into three large groups: Archaea, Bacteria, and Eukarya. The first two have prokaryotic cells, and the third contains all eukaryotes. A relatively sparse fossil record is available to help discern what the first members of each of these lineages looked like, so it is possible that all the events that led to the last common ancestor of extant eukaryotes will remain unknown. However, comparative biology of extant organisms and the limited fossil record provide some insight into the history of Eukarya.

The earliest fossils found appear to be Bacteria, most likely cyanobacteria. They are about 3.5 billion years old and are recognizable because of their relatively complex structure and, for prokaryotes, relatively large cells. Most other prokaryotes have small cells, 1 or 2 μm in size, and would be difficult to pick out as fossils. Most living eukaryotes have cells measuring 10 μm or greater. Structures this size, which might be fossils, appear in the geological record about 2.1 billion years ago.

Characteristics of Eukaryotes

Data from these fossils have led comparative biologists to the conclusion that living eukaryotes are all descendants of a single common ancestor. Mapping the characteristics found in all major groups of eukaryotes reveals that the following characteristics must have been present in the last common ancestor, because these characteristics are present in at least some of the members of each major lineage.

1. Cells with nuclei surrounded by a nuclear envelope with nuclear pores. This is the single characteristic that is both necessary and sufficient to define an organism as a eukaryote. All extant eukaryotes have cells with nuclei.

2. Mitochondria. Some extant eukaryotes have very reduced remnants of mitochondria in their cells, whereas other members of their lineages have “typical” mitochondria.
3. A cytoskeleton containing the structural and motility components called actin microfilaments and microtubules. All extant eukaryotes have these cytoskeletal elements.
4. Flagella and cilia, organelles associated with cell motility. Some extant eukaryotes lack flagella and/or cilia, but they are descended from ancestors that possessed them.
5. Chromosomes, each consisting of a linear DNA molecule coiled around basic (alkaline) proteins called histones. The few eukaryotes with chromosomes lacking histones clearly evolved from ancestors that had them.
6. Mitosis, a process of nuclear division wherein replicated chromosomes are divided and separated using elements of the cytoskeleton. Mitosis is universally present in eukaryotes.
7. Sex, a process of genetic recombination unique to eukaryotes in which diploid nuclei at one stage of the life cycle undergo meiosis to yield haploid nuclei and subsequent karyogamy, a stage where two haploid nuclei fuse together to create a diploid zygote nucleus.
8. Members of all major lineages have cell walls, and it might be reasonable to conclude that the last common ancestor could make cell walls during some stage of its life cycle. However, not enough is known about eukaryotes’ cell walls and their development to know how much homology exists among them. If the last common ancestor could make cell walls, it is clear that this ability must have been lost in many groups.

Endosymbiosis and the Evolution of Eukaryotes

In order to understand eukaryotic organisms fully, it is necessary to understand that all extant eukaryotes are descendants of a chimeric organism that was a composite of a host cell and the cell(s) of an alpha-proteobacterium that “took up residence” inside it. This major theme in the origin of eukaryotes is known as **endosymbiosis**, one cell engulfing another such that the engulfed cell survives and both cells benefit. Over many generations, a symbiotic relationship can result in two organisms that

depend on each other so completely that neither could survive on its own. Endosymbiotic events likely contributed to the origin of the last common ancestor of today's eukaryotes and to later diversification in certain lineages of eukaryotes ([\[link\]](#)). Before explaining this further, it is necessary to consider metabolism in prokaryotes.

Prokaryotic Metabolism

Many important metabolic processes arose in prokaryotes, and some of these, such as nitrogen fixation, are never found in eukaryotes. The process of aerobic respiration is found in all major lineages of eukaryotes, and it is localized in the mitochondria. Aerobic respiration is also found in many lineages of prokaryotes, but it is not present in all of them, and many forms of evidence suggest that such anaerobic prokaryotes never carried out aerobic respiration nor did their ancestors.

While today's atmosphere is about one-fifth molecular oxygen (O_2), geological evidence shows that it originally lacked O_2 . Without oxygen, aerobic respiration would not be expected, and living things would have relied on fermentation instead. At some point before, about 3.5 billion years ago, some prokaryotes began using energy from sunlight to power anabolic processes that reduce carbon dioxide to form organic compounds. That is, they evolved the ability to photosynthesize. Hydrogen, derived from various sources, was captured using light-powered reactions to reduce fixed carbon dioxide in the Calvin cycle. The group of Gram-negative bacteria that gave rise to cyanobacteria used water as the hydrogen source and released O_2 as a waste product.

Eventually, the amount of photosynthetic oxygen built up in some environments to levels that posed a risk to living organisms, since it can damage many organic compounds. Various metabolic processes evolved that protected organisms from oxygen, one of which, aerobic respiration, also generated high levels of ATP. It became widely present among prokaryotes, including in a group we now call alpha-proteobacteria. Organisms that did not acquire aerobic respiration had to remain in oxygen-free environments. Originally, oxygen-rich environments were likely

localized around places where cyanobacteria were active, but by about 2 billion years ago, geological evidence shows that oxygen was building up to higher concentrations in the atmosphere. Oxygen levels similar to today's levels only arose within the last 700 million years.

Recall that the first fossils that we believe to be eukaryotes date to about 2 billion years old, so they appeared as oxygen levels were increasing. Also, recall that all extant eukaryotes descended from an ancestor with mitochondria. These organelles were first observed by light microscopists in the late 1800s, where they appeared to be somewhat worm-shaped structures that seemed to be moving around in the cell. Some early observers suggested that they might be bacteria living inside host cells, but these hypotheses remained unknown or rejected in most scientific communities.

Endosymbiotic Theory

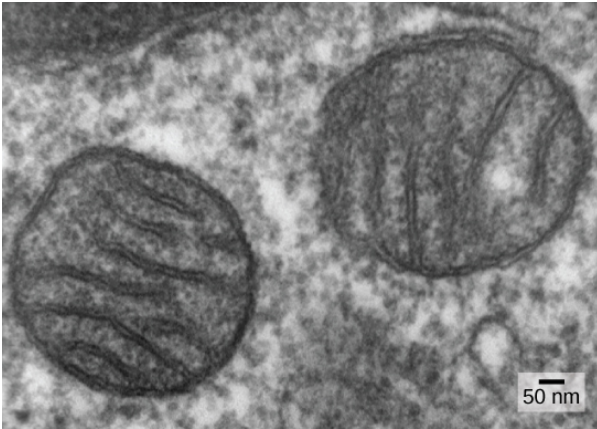
As cell biology developed in the twentieth century, it became clear that mitochondria were the organelles responsible for producing ATP using aerobic respiration. In the 1960s, American biologist Lynn Margulis developed **endosymbiotic theory**, which states that eukaryotes may have been a product of one cell engulfing another, one living within another, and evolving over time until the separate cells were no longer recognizable as such. In 1967, Margulis introduced new work on the theory and substantiated her findings through microbiological evidence. Although Margulis' work initially was met with resistance, this once-revolutionary hypothesis is now widely (but not completely) accepted, with work progressing on uncovering the steps involved in this evolutionary process and the key players involved. Much still remains to be discovered about the origins of the cells that now make up the cells in all living eukaryotes.

Broadly, it has become clear that many of our nuclear genes and the molecular machinery responsible for replication and expression appear closely related to those in Archaea. On the other hand, the metabolic organelles and genes responsible for many energy-harvesting processes had their origins in bacteria. Much remains to be clarified about how this

relationship occurred; this continues to be an exciting field of discovery in biology. For instance, it is not known whether the endosymbiotic event that led to mitochondria occurred before or after the host cell had a nucleus. Such organisms would be among the extinct precursors of the last common ancestor of eukaryotes.

Mitochondria

One of the major features distinguishing prokaryotes from eukaryotes is the presence of mitochondria. Eukaryotic cells may contain anywhere from one to several thousand mitochondria, depending on the cell's level of energy consumption. Each mitochondrion measures 1 to 10 or greater micrometers in length and exists in the cell as an organelle that can be ovoid to worm-shaped to intricately branched ([\[link\]](#)). Mitochondria arise from the division of existing mitochondria; they may fuse together; and they may be moved around inside the cell by interactions with the cytoskeleton. However, mitochondria cannot survive outside the cell. As the atmosphere was oxygenated by photosynthesis, and as successful aerobic prokaryotes evolved, evidence suggests that an ancestral cell with some membrane compartmentalization engulfed a free-living aerobic prokaryote, specifically an alpha-proteobacterium, thereby giving the host cell the ability to use oxygen to release energy stored in nutrients. Alpha-proteobacteria are a large group of bacteria that includes species symbiotic with plants, disease organisms that can infect humans via ticks, and many free-living species that use light for energy. Several lines of evidence support that mitochondria are derived from this endosymbiotic event. Most mitochondria are shaped like alpha-proteobacteria and are surrounded by two membranes, which would result when one membrane-bound organism was engulfed into a vacuole by another membrane-bound organism. The mitochondrial inner membrane is extensive and involves substantial infoldings called cristae that resemble the textured, outer surface of alpha-proteobacteria. The matrix and inner membrane are rich with the enzymes necessary for aerobic respiration.



In this transmission electron micrograph of mitochondria in a mammalian lung cell, the cristae, infoldings of the mitochondrial inner membrane, can be seen in cross-section.
(credit: Louise Howard)

Mitochondria divide independently by a process that resembles binary fission in prokaryotes. Specifically, mitochondria are not formed from scratch (de novo) by the eukaryotic cell; they reproduce within it and are distributed with the cytoplasm when a cell divides or two cells fuse. Therefore, although these organelles are highly integrated into the eukaryotic cell, they still reproduce as if they are independent organisms within the cell. However, their reproduction is synchronized with the activity and division of the cell. Mitochondria have their own (usually) circular DNA chromosome that is stabilized by attachments to the inner membrane and carries genes similar to genes expressed by alpha-proteobacteria. Mitochondria also have special ribosomes and transfer RNAs that resemble these components in prokaryotes. These features all support that mitochondria were once free-living prokaryotes.

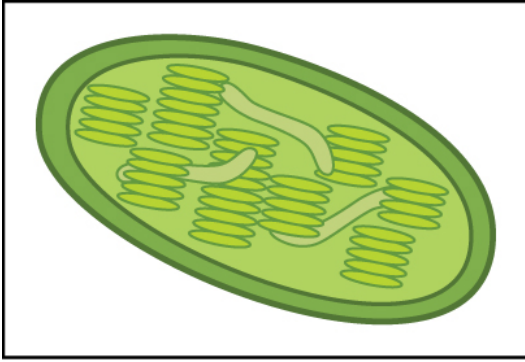
Mitochondria that carry out aerobic respiration have their own genomes, with genes similar to those in alpha-proteobacteria. However, many of the genes for respiratory proteins are located in the nucleus. When these genes

are compared to those of other organisms, they appear to be of alpha-proteobacterial origin. Additionally, in some eukaryotic groups, such genes are found in the mitochondria, whereas in other groups, they are found in the nucleus. This has been interpreted as evidence that genes have been transferred from the endosymbiont chromosome to the host genome. This loss of genes by the endosymbiont is probably one explanation why mitochondria cannot live without a host.

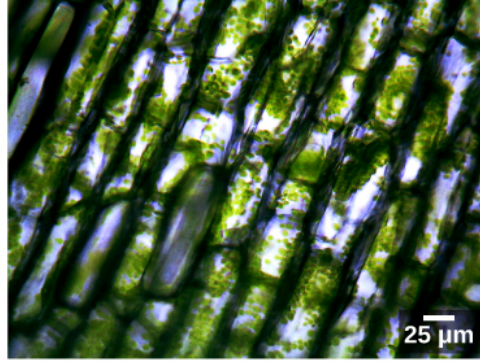
Some living eukaryotes are anaerobic and cannot survive in the presence of too much oxygen. Some appear to lack organelles that could be recognized as mitochondria. In the 1970s to the early 1990s, many biologists suggested that some of these eukaryotes were descended from ancestors whose lineages had diverged from the lineage of mitochondrion-containing eukaryotes before endosymbiosis occurred. However, later findings suggest that reduced organelles are found in most, if not all, anaerobic eukaryotes, and that all eukaryotes appear to carry some genes in their nuclei that are of mitochondrial origin. In addition to the aerobic generation of ATP, mitochondria have several other metabolic functions. One of these functions is to generate clusters of iron and sulfur that are important cofactors of many enzymes. Such functions are often associated with the reduced mitochondrion-derived organelles of anaerobic eukaryotes. Therefore, most biologists accept that the last common ancestor of eukaryotes had mitochondria.

Plastids

Some groups of eukaryotes are photosynthetic. Their cells contain, in addition to the standard eukaryotic organelles, another kind of organelle called a **plastid**. When such cells are carrying out photosynthesis, their plastids are rich in the pigment chlorophyll *a* and a range of other pigments, called accessory pigments, which are involved in harvesting energy from light. Photosynthetic plastids are called chloroplasts ([\[link\]](#)).



(a)



(b)

(a) This chloroplast cross-section illustrates its elaborate inner membrane organization. Stacks of thylakoid membranes compartmentalize photosynthetic enzymes and provide scaffolding for chloroplast DNA. (b) In this micrograph of *Elodea* sp., the chloroplasts can be seen as small green spheres. (credit b: modification of work by Brandon Zierer; scale-bar data from Matt Russell)

Like mitochondria, plastids appear to have an endosymbiotic origin. This hypothesis was also championed by Lynn Margulis. Plastids are derived from cyanobacteria that lived inside the cells of an ancestral, aerobic, heterotrophic eukaryote. This is called primary endosymbiosis, and plastids of primary origin are surrounded by two membranes. The best evidence is that this has happened twice in the history of eukaryotes. In one case, the common ancestor of the major lineage/supergroup Archaeplastida took on a cyanobacterial endosymbiont; in the other, the ancestor of the small amoeboid rhizarian taxon, *Paulinella*, took on a different cyanobacterial endosymbiont. Almost all photosynthetic eukaryotes are descended from the first event, and only a couple of species are derived from the other.

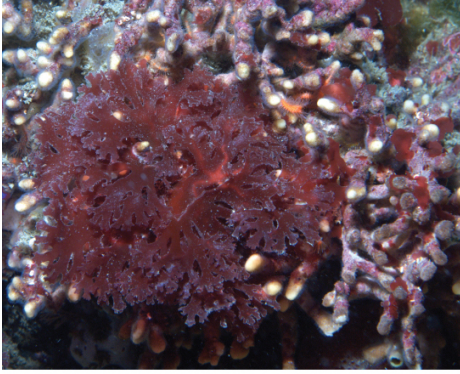
Cyanobacteria are a group of Gram-negative bacteria with all the conventional structures of the group. However, unlike most prokaryotes, they have extensive, internal membrane-bound sacs called thylakoids. Chlorophyll is a component of these membranes, as are many of the proteins of the light reactions of photosynthesis. Cyanobacteria also have

the peptidoglycan wall and lipopolysaccharide layer associated with Gram-negative bacteria.

Chloroplasts of primary origin have thylakoids, a circular DNA chromosome, and ribosomes similar to those of cyanobacteria. Each chloroplast is surrounded by two membranes. In the group of Archaeplastida called the glaucophytes and in *Paulinella*, a thin peptidoglycan layer is present between the outer and inner plastid membranes. All other plastids lack this relictual cyanobacterial wall. The outer membrane surrounding the plastid is thought to be derived from the vacuole in the host, and the inner membrane is thought to be derived from the plasma membrane of the symbiont.

There is also, as with the case of mitochondria, strong evidence that many of the genes of the endosymbiont were transferred to the nucleus. Plastids, like mitochondria, cannot live independently outside the host. In addition, like mitochondria, plastids are derived from the division of other plastids and never built from scratch. Researchers have suggested that the endosymbiotic event that led to Archaeplastida occurred 1 to 1.5 billion years ago, at least 5 hundred million years after the fossil record suggests that eukaryotes were present.

Not all plastids in eukaryotes are derived directly from primary endosymbiosis. Some of the major groups of algae became photosynthetic by secondary endosymbiosis, that is, by taking in either green algae or red algae (both from Archaeplastida) as endosymbionts ([link](#)ab). Numerous microscopic and genetic studies have supported this conclusion. Secondary plastids are surrounded by three or more membranes, and some secondary plastids even have clear remnants of the nucleus of endosymbiotic alga. Others have not “kept” any remnants. There are cases where tertiary or higher-order endosymbiotic events are the best explanations for plastids in some eukaryotes.



(a)



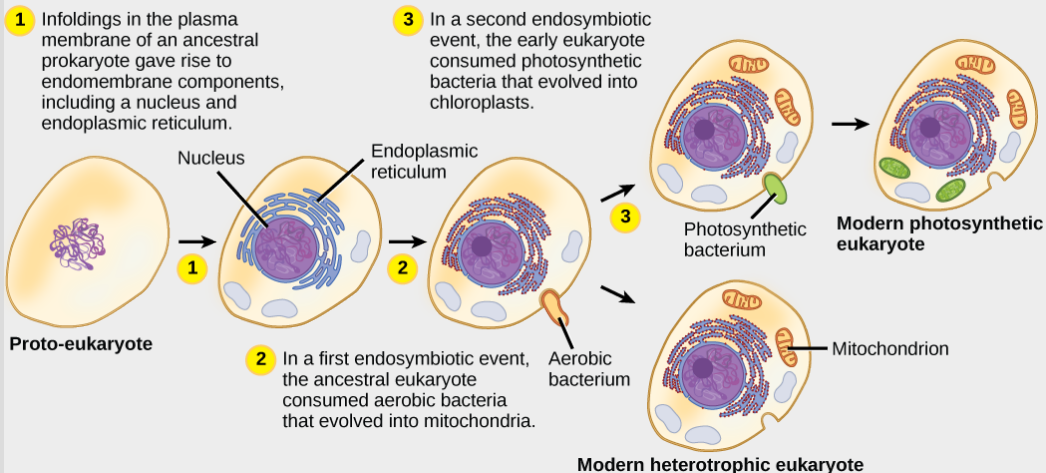
(b)

(a) Red algae and (b) green algae (visualized by light microscopy) share similar DNA sequences with photosynthetic cyanobacteria. Scientists speculate that, in a process called endosymbiosis, an ancestral prokaryote engulfed a photosynthetic cyanobacterium that evolved into modern-day chloroplasts. (credit a: modification of work by Ed Bierman; credit b: modification of work by G. Fahnenstiel, NOAA; scale-bar data from Matt Russell)

Note:

Art Connection

The ENDOSYMBIOTIC THEORY



The first eukaryote may have originated from an ancestral prokaryote that had undergone membrane proliferation, compartmentalization of cellular function (into a nucleus, lysosomes, and an endoplasmic reticulum), and the establishment of endosymbiotic relationships with an aerobic prokaryote, and, in some cases, a photosynthetic prokaryote, to form mitochondria and chloroplasts, respectively.

What evidence is there that mitochondria were incorporated into the ancestral eukaryotic cell before chloroplasts?

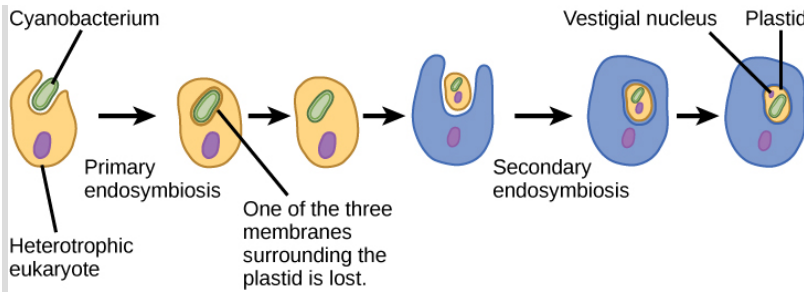
Note:

Evolution Connection

Secondary Endosymbiosis in Chlorarachniophytes

Endosymbiosis involves one cell engulfing another to produce, over time, a coevolved relationship in which neither cell could survive alone. The chloroplasts of red and green algae, for instance, are derived from the engulfment of a photosynthetic cyanobacterium by an early prokaryote. This leads to the question of the possibility of a cell containing an endosymbiont to itself become engulfed, resulting in a secondary endosymbiosis. Molecular and morphological evidence suggest that the chlorarachniophyte protists are derived from a secondary endosymbiotic event. Chlorarachniophytes are rare algae indigenous to tropical seas and sand that can be classified into the rhizarian supergroup.

Chlorarachniophytes extend thin cytoplasmic strands, interconnecting themselves with other chlorarachniophytes, in a cytoplasmic network. These protists are thought to have originated when a eukaryote engulfed a green alga, the latter of which had already established an endosymbiotic relationship with a photosynthetic cyanobacterium ([\[link\]](#)).



The hypothesized process of endosymbiotic events leading to the evolution of chlorarachniophytes is shown. In a primary endosymbiotic event, a heterotrophic eukaryote consumed a cyanobacterium. In a secondary endosymbiotic event, the cell resulting from primary endosymbiosis was consumed by a second cell. The resulting organelle became a plastid in modern chlorarachniophytes.

Several lines of evidence support that chlorarachniophytes evolved from secondary endosymbiosis. The chloroplasts contained within the green algal endosymbionts still are capable of photosynthesis, making chlorarachniophytes photosynthetic. The green algal endosymbiont also exhibits a stunted vestigial nucleus. In fact, it appears that chlorarachniophytes are the products of an evolutionarily recent secondary endosymbiotic event. The plastids of chlorarachniophytes are surrounded by four membranes: The first two correspond to the inner and outer membranes of the photosynthetic cyanobacterium, the third corresponds to the green alga, and the fourth corresponds to the vacuole that surrounded the green alga when it was engulfed by the chlorarachniophyte ancestor. In other lineages that involved secondary endosymbiosis, only three membranes can be identified around plastids. This is currently rectified as a sequential loss of a membrane during the course of evolution. The process of secondary endosymbiosis is not unique to chlorarachniophytes. In fact, secondary endosymbiosis of green algae also led to euglenid protists, whereas secondary endosymbiosis of red algae led to the evolution of dinoflagellates, apicomplexans, and stramenopiles.

Section Summary

The oldest fossil evidence of eukaryotes is about 2 billion years old. Fossils older than this all appear to be prokaryotes. It is probable that today's eukaryotes are descended from an ancestor that had a prokaryotic organization. The last common ancestor of today's Eukarya had several characteristics, including cells with nuclei that divided mitotically and contained linear chromosomes where the DNA was associated with histones, a cytoskeleton and endomembrane system, and the ability to make cilia/flagella during at least part of its life cycle. It was aerobic because it had mitochondria that were the result of an aerobic alpha-proteobacterium that lived inside a host cell. Whether this host had a nucleus at the time of the initial symbiosis remains unknown. The last common ancestor may have had a cell wall for at least part of its life cycle, but more data are needed to confirm this hypothesis. Today's eukaryotes are very diverse in their shapes, organization, life cycles, and number of cells per individual.

Art Connections

Exercise:

Problem:

[\[link\]](#) What evidence is there that mitochondria were incorporated into the ancestral eukaryotic cell before chloroplasts?

Solution:

[\[link\]](#) All eukaryotic cells have mitochondria, but not all eukaryotic cells have chloroplasts.

Review Questions

Exercise:

Problem:

What event is thought to have contributed to the evolution of eukaryotes?

- a. global warming
- b. glaciation
- c. volcanic activity
- d. oxygenation of the atmosphere

Solution:

D

Exercise:

Problem:

Which characteristic is shared by prokaryotes and eukaryotes?

- a. cytoskeleton
- b. nuclear envelope
- c. DNA-based genome
- d. mitochondria

Solution:

C

Exercise:

Problem: Mitochondria most likely evolved by _____.

- a. a photosynthetic cyanobacterium
- b. cytoskeletal elements
- c. endosymbiosis
- d. membrane proliferation

Solution:

C

Exercise:**Problem:**

Which of these protists is believed to have evolved following a secondary endosymbiosis?

- a. green algae
- b. cyanobacteria
- c. red algae
- d. chlorarachniophytes

Solution:

D

Free Response**Exercise:****Problem:**

Describe the hypothesized steps in the origin of eukaryotic cells.

Solution:

Eukaryotic cells arose through endosymbiotic events that gave rise to the energy-producing organelles within the eukaryotic cells such as mitochondria and chloroplasts. The nuclear genome of eukaryotes is related most closely to the Archaea, so it may have been an early archaean that engulfed a bacterial cell that evolved into a mitochondrion. Mitochondria appear to have originated from an alpha-proteobacterium, whereas chloroplasts originated as a cyanobacterium.

There is also evidence of secondary endosymbiotic events. Other cell components may also have resulted from endosymbiotic events.

Glossary

endosymbiosis

engulfment of one cell within another such that the engulfed cell survives, and both cells benefit; the process responsible for the evolution of mitochondria and chloroplasts in eukaryotes

endosymbiotic theory

theory that states that eukaryotes may have been a product of one cell engulfing another, one living within another, and evolving over time until the separate cells were no longer recognizable as such

plastid

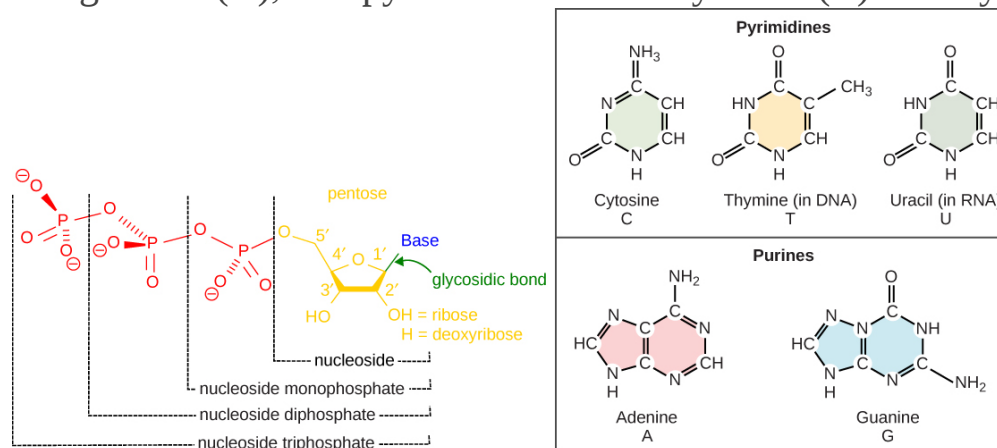
one of a group of related organelles in plant cells that are involved in the storage of starches, fats, proteins, and pigments

Bis2A 11.0 DNA Structure

By the end of this section, you will be able to:

- Describe the structure of DNA
- Explain the Sanger method of DNA sequencing
- Discuss the similarities and differences between eukaryotic and prokaryotic DNA

The building blocks of DNA are nucleotides. The important components of the nucleotide are a nitrogenous base, deoxyribose (5-carbon sugar), and a phosphate group ([\[link\]](#)). The nucleotide is named depending on the nitrogenous base. The nitrogenous base can be a purine such as adenine (A) and guanine (G), or a pyrimidine such as cytosine (C) and thymine (T).



Each nucleotide is made up of a sugar, a phosphate group, and a nitrogenous base. The sugar is deoxyribose in DNA and ribose in RNA.

The nucleotides combine with each other by covalent bonds known as phosphodiester bonds or linkages. The purines have a double ring structure with a six-membered ring fused to a five-membered ring. Pyrimidines are smaller in size; they have a single six-membered ring structure. The carbon atoms of the five-carbon sugar are numbered 1', 2', 3', 4', and 5' (1' is read as "one prime"). The phosphate residue is attached to the hydroxyl group of the 5' carbon of one sugar of one nucleotide and the hydroxyl group of the

3' carbon of the sugar of the next nucleotide, thereby forming a 5'-3' phosphodiester bond.

In the 1950s, Francis Crick and James Watson worked together to determine the structure of DNA at the University of Cambridge, England. Other scientists like Linus Pauling and Maurice Wilkins were also actively exploring this field. Pauling had discovered the secondary structure of proteins using X-ray crystallography. In Wilkins' lab, researcher Rosalind Franklin was using X-ray diffraction methods to understand the structure of DNA. Watson and Crick were able to piece together the puzzle of the DNA molecule on the basis of Franklin's data because Crick had also studied X-ray diffraction ([\[link\]](#)). In 1962, James Watson, Francis Crick, and Maurice Wilkins were awarded the Nobel Prize in Medicine. Unfortunately, by then Franklin had died, and Nobel prizes are not awarded posthumously.



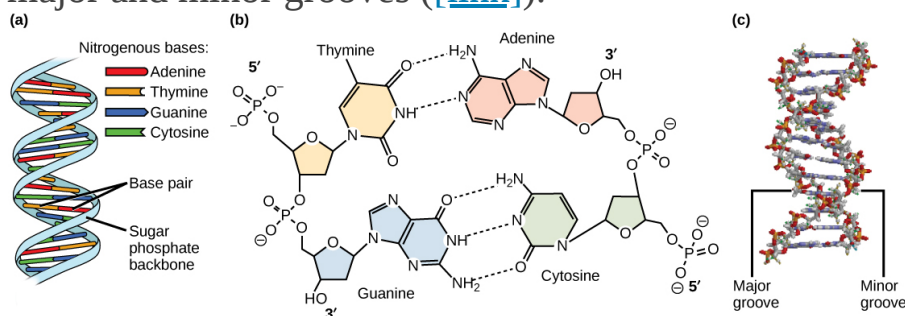
(a)



(b)

The work of pioneering scientists (a) James Watson, Francis Crick, and Maclyn McCarty led to our present day understanding of DNA. Scientist Rosalind Franklin discovered (b) the X-ray diffraction pattern of DNA, which helped to elucidate its double helix structure. (credit a: modification of work by Marjorie McCarty, Public Library of Science)

Watson and Crick proposed that DNA is made up of two strands that are twisted around each other to form a right-handed helix. Base pairing takes place between a purine and pyrimidine; namely, A pairs with T and G pairs with C. Adenine and thymine are complementary base pairs, and cytosine and guanine are also complementary base pairs. The base pairs are stabilized by hydrogen bonds; adenine and thymine form two hydrogen bonds and cytosine and guanine form three hydrogen bonds. The two strands are anti-parallel in nature; that is, the 3' end of one strand faces the 5' end of the other strand. The sugar and phosphate of the nucleotides form the backbone of the structure, whereas the nitrogenous bases are stacked inside. Each base pair is separated from the other base pair by a distance of 0.34 nm, and each turn of the helix measures 3.4 nm. Therefore, ten base pairs are present per turn of the helix. The diameter of the DNA double helix is 2 nm, and it is uniform throughout. Only the pairing between a purine and pyrimidine can explain the uniform diameter. The twisting of the two strands around each other results in the formation of uniformly spaced major and minor grooves ([\[link\]](#)).



DNA has (a) a double helix structure and (b) phosphodiester bonds. The (c) major and minor grooves are binding sites for DNA binding proteins during processes such as transcription (the copying of RNA from DNA) and replication.

Section Summary

The currently accepted model of the double-helix structure of DNA was proposed by Watson and Crick. Some of the salient features are that the two

strands that make up the double helix are complementary and anti-parallel in nature. Deoxyribose sugars and phosphates form the backbone of the structure, and the nitrogenous bases are stacked inside. The diameter of the double helix, 2 nm, is uniform throughout. A purine always pairs with a pyrimidine; A pairs with T, and G pairs with C. One turn of the helix has ten base pairs. During cell division, each daughter cell receives a copy of the DNA by a process known as DNA replication. Prokaryotes are much simpler than eukaryotes in many of their features. Most prokaryotes contain a single, circular chromosome. In general, eukaryotic chromosomes contain a linear DNA molecule packaged into nucleosomes, and have two distinct regions that can be distinguished by staining, reflecting different states of packaging and compaction.

Review Questions

Exercise:

Problem: DNA double helix does not have which of the following?

- a. antiparallel configuration
- b. complementary base pairing
- c. major and minor grooves
- d. uracil

Solution:

D

Free Response

Exercise:

Problem:

Describe the structure and complementary base pairing of DNA.

Solution:

DNA has two strands in anti-parallel orientation. The sugar-phosphate linkages form a backbone on the outside, and the bases are paired on the inside: A with T, and G with C, like rungs on a spiral ladder.

Glossary

electrophoresis

technique used to separate DNA fragments according to size

Bis2A 11.1 DNA Synthesis

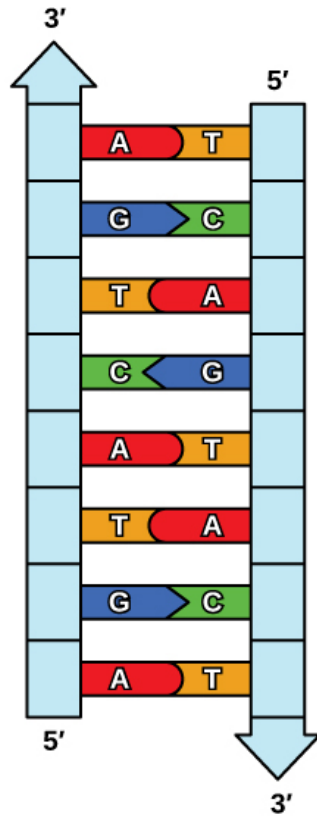
By the end of this section, you will be able to:

- Explain the process of DNA replication
- Explain the importance of telomerase to DNA replication
- Describe mechanisms of DNA repair

DNA Replication an overview

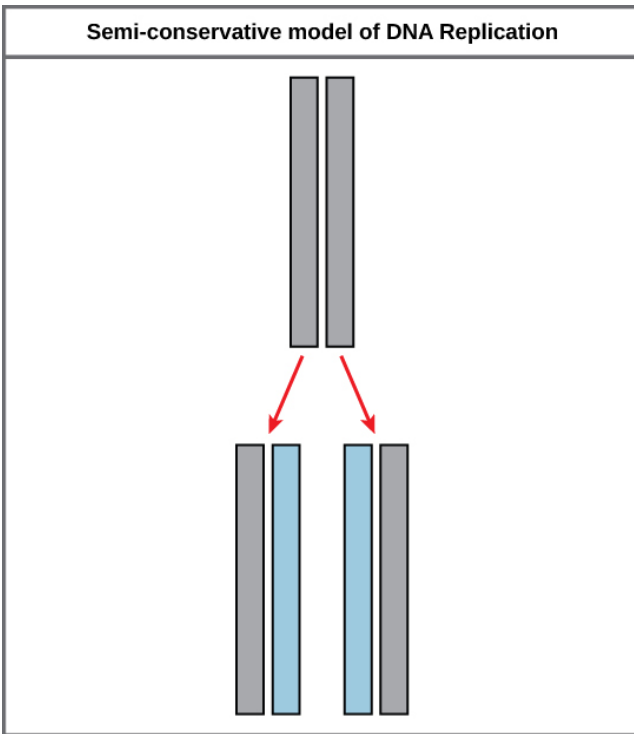
When a cell divides, it is important that each daughter cell receives an identical copy of the DNA. This is accomplished by the process of DNA replication. In Eukaryotic cells the replication of DNA occurs during the synthesis phase, or S phase, of the cell cycle, before the cell enters mitosis or meiosis, a subject we will discuss later in the quarter. In bacteria and archaea, DNA replication is regulated by the cell's energy demands and biomass. Regardless of how the process is regulated, the synthesis of DNA is a similar process, though the proteins and machinery used by each varies.

The elucidation of the structure of the double helix provided a hint as to how DNA is copied. Recall that adenine nucleotides pair with thymine nucleotides, and cytosine with guanine. This means that the two strands are complementary to each other. For example, a strand of DNA with a nucleotide sequence of AGTCATGA will have a complementary strand with the sequence TCAGTACT ([\[link\]](#)).



The two strands of DNA are complementary, meaning the sequence of bases in one strand can be used to create the correct sequence of bases in the other strand.

Because of the complementarity of the two strands, having one strand means that it is possible to recreate the other strand. This model for replication suggests that the two strands of the double helix separate during replication, and each strand serves as a template from which the new complementary strand is copied ([link](#)).



The semiconservative model of DNA replication is shown. Gray indicates the original DNA strands, and blue indicates newly synthesized DNA.

During DNA replication, each of the two strands that make up the double helix serves as a template from which new strands are copied. The new strand will be complementary to the parental or “old” strand. Each new double strand consists of one parental strand and one new daughter strand. This is known as **semiconservative replication**. When two DNA copies are formed, they have an identical sequence of nucleotide bases and are divided equally into two daughter cells.

DNA Replication in Eukaryotes

Because eukaryotic genomes are very complex, DNA replication is a very complicated process that involves several enzymes and other proteins. It

occurs in three main stages: initiation, elongation, and termination.

Recall that eukaryotic DNA is bound to proteins known as histones to form structures called nucleosomes. During initiation, the DNA is made accessible to the proteins and enzymes involved in the replication process. How does the replication machinery know where on the DNA double helix to begin? It turns out that there are specific nucleotide sequences called origins of replication at which replication begins. Certain proteins bind to the origin of replication while an enzyme called **helicase** unwinds and opens up the DNA helix. As the DNA opens up, Y-shaped structures called **replication forks** are formed ([\[link\]](#)). Two replication forks are formed at the origin of replication, and these get extended in both directions as replication proceeds. There are multiple origins of replication on the eukaryotic chromosome, such that replication can occur simultaneously from several places in the genome.

During elongation, an enzyme called **DNA polymerase** adds DNA nucleotides to the 3' end of the template. Because DNA polymerase can only add new nucleotides at the end of a backbone, a **primer** sequence, which provides this starting point, is added with complementary RNA nucleotides. This primer is removed later, and the nucleotides are replaced with DNA nucleotides. One strand, which is complementary to the parental DNA strand, is synthesized continuously toward the replication fork so the polymerase can add nucleotides in this direction. This continuously synthesized strand is known as the **leading strand**. Because DNA polymerase can only synthesize DNA in a 5' to 3' direction, the other new strand is put together in short pieces called **Okazaki fragments**. The Okazaki fragments each require a primer made of RNA to start the synthesis. The strand with the Okazaki fragments is known as the **lagging strand**. As synthesis proceeds, an enzyme removes the RNA primer, which is then replaced with DNA nucleotides, and the gaps between fragments are sealed by an enzyme called **DNA ligase**.

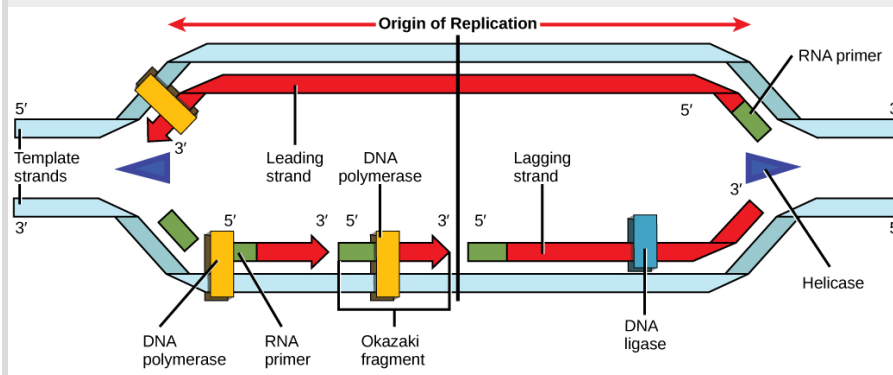
The process of DNA replication can be summarized as follows:

1. DNA unwinds at the origin of replication.
2. New bases are added to the complementary parental strands. One new strand is made continuously, while the other strand is made in pieces.

3. Primers are removed, new DNA nucleotides are put in place of the primers and the backbone is sealed by DNA ligase.

Note:

Art Connection



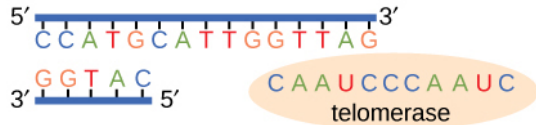
A replication fork is formed by the opening of the origin of replication, and helicase separates the DNA strands. An RNA primer is synthesized, and is elongated by the DNA polymerase. On the leading strand, DNA is synthesized continuously, whereas on the lagging strand, DNA is synthesized in short stretches. The DNA fragments are joined by DNA ligase (not shown).

You isolate a cell strain in which the joining together of Okazaki fragments is impaired and suspect that a mutation has occurred in an enzyme found at the replication fork. Which enzyme is most likely to be mutated?

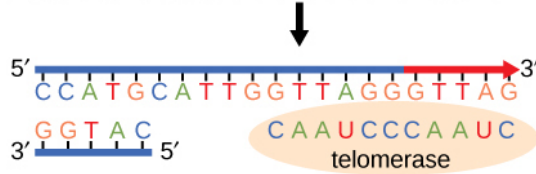
Telomere Replication

Because eukaryotic chromosomes are linear, DNA replication comes to the end of a line in eukaryotic chromosomes. As you have learned, the DNA polymerase enzyme can add nucleotides in only one direction. In the

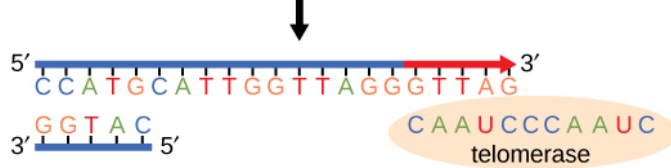
leading strand, synthesis continues until the end of the chromosome is reached; however, on the lagging strand there is no place for a primer to be made for the DNA fragment to be copied at the end of the chromosome. This presents a problem for the cell because the ends remain unpaired, and over time these ends get progressively shorter as cells continue to divide. The ends of the linear chromosomes are known as **telomeres**, which have repetitive sequences that do not code for a particular gene. As a consequence, it is telomeres that are shortened with each round of DNA replication instead of genes. For example, in humans, a six base-pair sequence, TTAGGG, is repeated 100 to 1000 times. The discovery of the enzyme **telomerase** ([\[link\]](#)) helped in the understanding of how chromosome ends are maintained. The telomerase attaches to the end of the chromosome, and complementary bases to the RNA template are added on the end of the DNA strand. Once the lagging strand template is sufficiently elongated, DNA polymerase can now add nucleotides that are complementary to the ends of the chromosomes. Thus, the ends of the chromosomes are replicated.



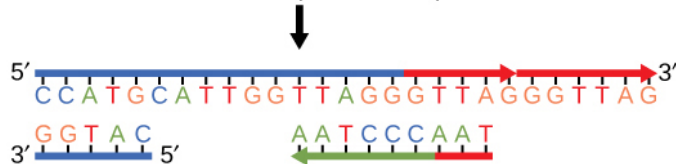
Telomerase has an associated RNA that complements the 3' overhang at the end of the chromosome.



The RNA template is used to synthesize the complementary strand.



Telomerase shifts, and the process is repeated.



Primase and DNA polymerase synthesize the complementary strand.

The ends of linear chromosomes are maintained by the action of the telomerase enzyme.

Telomerase is typically found to be active in germ cells, adult stem cells, and some cancer cells. For her discovery of telomerase and its action, Elizabeth Blackburn ([\[link\]](#)) received the Nobel Prize for Medicine and Physiology in 2009.



Elizabeth Blackburn, 2009 Nobel Laureate, was the scientist who discovered how telomerase works. (credit: U.S. Embassy, Stockholm, Sweden)

Telomerase is not active in adult somatic cells. Adult somatic cells that undergo cell division continue to have their telomeres shortened. This essentially means that telomere shortening is associated with aging. In 2010, scientists found that telomerase can reverse some age-related conditions in mice, and this may have potential in regenerative medicine. [\[footnote\]](#) Telomerase-deficient mice were used in these studies; these mice have tissue atrophy, stem-cell depletion, organ system failure, and impaired tissue injury responses. Telomerase reactivation in these mice caused extension of telomeres, reduced DNA damage, reversed neurodegeneration, and improved functioning of the testes, spleen, and intestines. Thus, telomere reactivation may have potential for treating age-related diseases in humans.

Mariella Jaskelioff, et al., “Telomerase reactivation reverses tissue degeneration in aged telomerase-deficient mice,” *Nature*, 469 (2011):102–7.

DNA Replication in Prokaryotes

Recall that the prokaryotic chromosome is a circular molecule with a less extensive coiling structure than eukaryotic chromosomes. The eukaryotic chromosome is linear and highly coiled around proteins. While there are many similarities in the DNA replication process, these structural differences necessitate some differences in the DNA replication process in these two life forms.

DNA replication has been extremely well-studied in prokaryotes, primarily because of the small size of the genome and large number of variants available. *Escherichia coli* has 4.6 million base pairs in a single circular chromosome, and all of it gets replicated in approximately 42 minutes, starting from a single origin of replication and proceeding around the chromosome in both directions. This means that approximately 1000 nucleotides are added per second. The process is much more rapid than in eukaryotes. [\[link\]](#) summarizes the differences between prokaryotic and eukaryotic replications.

Differences between Prokaryotic and Eukaryotic Replications		
Property	Prokaryotes	Eukaryotes
Origin of replication	Single	Multiple
Rate of replication	1000 nucleotides/s	50 to 100 nucleotides/s
Chromosome structure	circular	linear
Telomerase	Not present	Present

Note:**Concept in Action**

Click through a [tutorial](#) on DNA replication.

Section Summary

DNA replicates by a semi-conservative method in which each of the two parental DNA strands act as a template for new DNA to be synthesized. After replication, each DNA has one parental or “old” strand, and one daughter or “new” strand.

Replication in eukaryotes starts at multiple origins of replication, while replication in prokaryotes starts from a single origin of replication. The DNA is opened with enzymes, resulting in the formation of the replication fork. Primase synthesizes an RNA primer to initiate synthesis by DNA polymerase, which can add nucleotides in only one direction. One strand is synthesized continuously in the direction of the replication fork; this is called the leading strand. The other strand is synthesized in a direction away from the replication fork, in short stretches of DNA known as Okazaki fragments. This strand is known as the lagging strand. Once replication is completed, the RNA primers are replaced by DNA nucleotides and the DNA is sealed with DNA ligase.

The ends of eukaryotic chromosomes pose a problem, as polymerase is unable to extend them without a primer. Telomerase, an enzyme with an inbuilt RNA template, extends the ends by copying the RNA template and extending one end of the chromosome. DNA polymerase can then extend the DNA using the primer. In this way, the ends of the chromosomes are

protected. Cells have mechanisms for repairing DNA when it becomes damaged or errors are made in replication. These mechanisms include mismatch repair to replace nucleotides that are paired with a non-complementary base and nucleotide excision repair, which removes bases that are damaged such as thymine dimers.

Art Connections

Exercise:

Problem:

[\[link\]](#) You isolate a cell strain in which the joining together of Okazaki fragments is impaired and suspect that a mutation has occurred in an enzyme found at the replication fork. Which enzyme is most likely to be mutated?

Solution:

[\[link\]](#) Ligase, as this enzyme joins together Okazaki fragments.

Multiple Choice

Exercise:

Problem: DNA replicates by which of the following models?

- a. conservative
- b. semiconservative
- c. dispersive
- d. none of the above

Solution:

B

Exercise:**Problem:**

The initial mechanism for repairing nucleotide errors in DNA is _____.

- a. mismatch repair
- b. DNA polymerase proofreading
- c. nucleotide excision repair
- d. thymine dimers

Solution:

B

Free Response**Exercise:****Problem:**

How do the linear chromosomes in eukaryotes ensure that its ends are replicated completely?

Solution:

Telomerase has an inbuilt RNA template that extends the 3' end, so a primer is synthesized and extended. Thus, the ends are protected.

Glossary

DNA ligase

the enzyme that catalyzes the joining of DNA fragments together

DNA polymerase

an enzyme that synthesizes a new strand of DNA complementary to a template strand

helicase

an enzyme that helps to open up the DNA helix during DNA replication by breaking the hydrogen bonds

lagging strand

during replication of the 3' to 5' strand, the strand that is replicated in short fragments and away from the replication fork

leading strand

the strand that is synthesized continuously in the 5' to 3' direction that is synthesized in the direction of the replication fork

mismatch repair

a form of DNA repair in which non-complementary nucleotides are recognized, excised, and replaced with correct nucleotides

mutation

a permanent variation in the nucleotide sequence of a genome

nucleotide excision repair

a form of DNA repair in which the DNA molecule is unwound and separated in the region of the nucleotide damage, the damaged nucleotides are removed and replaced with new nucleotides using the complementary strand, and the DNA strand is resealed and allowed to rejoin its complement

Okazaki fragments

the DNA fragments that are synthesized in short stretches on the lagging strand

primer

a short stretch of RNA nucleotides that is required to initiate replication and allow DNA polymerase to bind and begin replication

replication fork

the Y-shaped structure formed during the initiation of replication

semiconservative replication

the method used to replicate DNA in which the double-stranded molecule is separated and each strand acts as a template for a new strand to be synthesized, so the resulting DNA molecules are composed of one new strand of nucleotides and one old strand of nucleotides

telomerase

an enzyme that contains a catalytic part and an inbuilt RNA template; it functions to maintain telomeres at chromosome ends

telomere

the DNA at the end of linear chromosomes

Bis2A 11.2 Mutations and DNA Repair

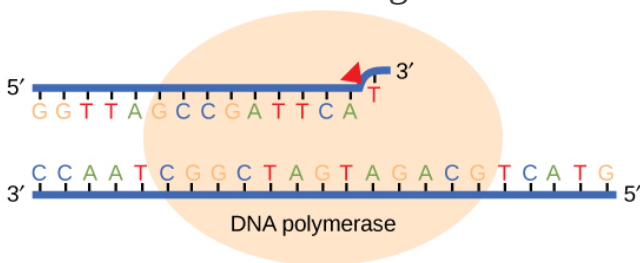
By the end of this section, you will be able to:

- Discuss the different types of mutations in DNA
- Explain DNA repair mechanisms

What happens when DNA synthesis goes wrong?

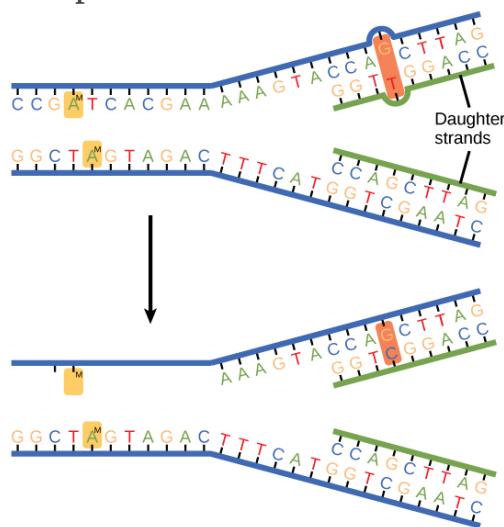
DNA replication is a highly accurate process, but mistakes can occasionally occur, such as a DNA polymerase inserting a wrong base. Uncorrected mistakes may sometimes lead to serious consequences, such as cancer. Repair mechanisms correct the mistakes. In rare cases, mistakes are not corrected, leading to mutations; in other cases, repair enzymes are themselves mutated or defective.

Most of the mistakes during DNA replication are promptly corrected by DNA polymerase by proofreading the base that has been just added ([\[link\]](#)). In **proofreading**, the DNA pol reads the newly added base before adding the next one, so a correction can be made. The polymerase checks whether the newly added base has paired correctly with the base in the template strand. If it is the right base, the next nucleotide is added. If an incorrect base has been added, the enzyme makes a cut at the phosphodiester bond and releases the wrong nucleotide. This is performed by the exonuclease action of DNA pol III. Once the incorrect nucleotide has been removed, a new one will be added again.



Proofreading by DNA polymerase corrects errors during replication.

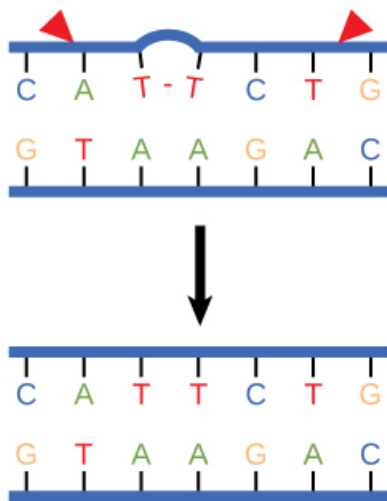
Some errors are not corrected during replication, but are instead corrected after replication is completed; this type of repair is known as **mismatch repair** ([\[link\]](#)). The enzymes recognize the incorrectly added nucleotide and excise it; this is then replaced by the correct base. If this remains uncorrected, it may lead to more permanent damage. How do mismatch repair enzymes recognize which of the two bases is the incorrect one? In *E. coli*, after replication, the nitrogenous base adenine acquires a methyl group; the parental DNA strand will have methyl groups, whereas the newly synthesized strand lacks them. Thus, DNA polymerase is able to remove the wrongly incorporated bases from the newly synthesized, non-methylated strand. In eukaryotes, the mechanism is not very well understood, but it is believed to involve recognition of unsealed nicks in the new strand, as well as a short-term continuing association of some of the replication proteins with the new daughter strand after replication has completed.



In mismatch repair, the incorrectly added base is detected after replication.

The mismatch repair proteins detect this base and remove it from the newly synthesized strand by nuclease action. The gap is now filled with the correctly paired base.

In another type of repair mechanism, **nucleotide excision repair**, enzymes replace incorrect bases by making a cut on both the 3' and 5' ends of the incorrect base ([\[link\]](#)). The segment of DNA is removed and replaced with the correctly paired nucleotides by the action of DNA pol. Once the bases are filled in, the remaining gap is sealed with a phosphodiester linkage catalyzed by DNA ligase. This repair mechanism is often employed when UV exposure causes the formation of pyrimidine dimers.



Nucleotide excision repairs thymine dimers. When exposed to UV, thymine dimers can form. In normal cells, they are excised and replaced.

A well-studied example of mistakes not being corrected is seen in people suffering from xeroderma pigmentosa ([link](#)). Affected individuals have skin that is highly sensitive to UV rays from the sun. When individuals are exposed to UV, pyrimidine dimers, especially those of thymine, are formed; people with xeroderma pigmentosa are not able to repair the damage. These are not repaired because of a defect in the nucleotide excision repair enzymes, whereas in normal individuals, the thymine dimers are excised and the defect is corrected. The thymine dimers distort the structure of the DNA double helix, and this may cause problems during DNA replication. People with xeroderma pigmentosa may have a higher risk of contracting skin cancer than those who don't have the condition.



Xeroderma pigmentosa is a condition in which thymine dimerization from exposure to UV is not repaired. Exposure to sunlight results in skin lesions.
(credit: James Halpern et al.)

Errors during DNA replication are not the only reason why mutations arise in DNA. **Mutations**, variations in the nucleotide sequence of a genome, can also occur because of damage to DNA. Such mutations may be of two types: induced or spontaneous. **Induced mutations** are those that result

from an exposure to chemicals, UV rays, x-rays, or some other environmental agent. **Spontaneous mutations** occur without any exposure to any environmental agent; they are a result of natural reactions taking place within the body.

Mutations may have a wide range of effects. Some mutations are not expressed; these are known as **silent mutations**. **Point mutations** are those mutations that affect a single base pair. The most common nucleotide mutations are substitutions, in which one base is replaced by another. These can be of two types, either transitions or transversions. **Transition substitution** refers to a purine or pyrimidine being replaced by a base of the same kind; for example, a purine such as adenine may be replaced by the purine guanine. **Transversion substitution** refers to a purine being replaced by a pyrimidine, or vice versa; for example, cytosine, a pyrimidine, is replaced by adenine, a purine. Mutations can also be the result of the addition of a base, known as an insertion, or the removal of a base, also known as deletion. Sometimes a piece of DNA from one chromosome may get translocated to another chromosome or to another region of the same chromosome; this is also known as translocation. These mutation types are shown in [\[link\]](#).

Note:

Art Connection

Point Mutations

Silent: has no effect on the protein sequence



Missense: results in an amino acid substitution

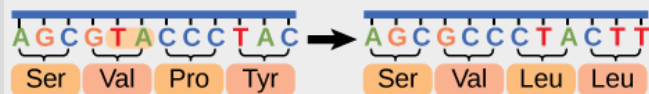


Nonsense: substitutes a stop codon for an amino acid



Frameshift Mutations

Insertions or deletions of nucleotides may result in a shift in the reading frame or insertion of a stop codon.



Mutations can lead to changes in the protein sequence encoded by the DNA.

A frameshift mutation that results in the insertion of three nucleotides is often less deleterious than a mutation that results in the insertion of one nucleotide. Why?

Mutations in repair genes have been known to cause cancer. Many mutated repair genes have been implicated in certain forms of pancreatic cancer, colon cancer, and colorectal cancer. Mutations can affect either somatic cells or germ cells. If many mutations accumulate in a somatic cell, they may lead to problems such as the uncontrolled cell division observed in cancer. If a mutation takes place in germ cells, the mutation will be passed

on to the next generation, as in the case of hemophilia and xeroderma pigmentosa.

Section Summary

DNA polymerase can make mistakes while adding nucleotides. It edits the DNA by proofreading every newly added base. Incorrect bases are removed and replaced by the correct base, and then a new base is added. Most mistakes are corrected during replication, although when this does not happen, the mismatch repair mechanism is employed. Mismatch repair enzymes recognize the wrongly incorporated base and excise it from the DNA, replacing it with the correct base. In yet another type of repair, nucleotide excision repair, the incorrect base is removed along with a few bases on the 5' and 3' end, and these are replaced by copying the template with the help of DNA polymerase. The ends of the newly synthesized fragment are attached to the rest of the DNA using DNA ligase, which creates a phosphodiester bond.

Most mistakes are corrected, and if they are not, they may result in a mutation defined as a permanent change in the DNA sequence. Mutations can be of many types, such as substitution, deletion, insertion, and translocation. Mutations in repair genes may lead to serious consequences such as cancer. Mutations can be induced or may occur spontaneously.

Art Connections

Exercise:

Problem:

[\[link\]](#) A frameshift mutation that results in the insertion of three nucleotides is often less deleterious than a mutation that results in the insertion of one nucleotide. Why?

Solution:

[\[link\]](#) If three nucleotides are added, one additional amino acid will be incorporated into the protein chain, but the reading frame won't shift.

Review Questions

Exercise:

Problem:

During proofreading, which of the following enzymes reads the DNA?

- a. primase
- b. topoisomerase
- c. DNA pol
- d. helicase

Solution:

C

Exercise:

Problem:

The initial mechanism for repairing nucleotide errors in DNA is _____.

- a. mismatch repair
- b. DNA polymerase proofreading
- c. nucleotide excision repair
- d. thymine dimers

Solution:

B

Free Response

Exercise:

Problem:

What is the consequence of mutation of a mismatch repair enzyme?
How will this affect the function of a gene?

Solution:

Mutations are not repaired, as in the case of xeroderma pigmentosa.
Gene function may be affected or it may not be expressed.

Glossary

induced mutation

mutation that results from exposure to chemicals or environmental agents

mutation

variation in the nucleotide sequence of a genome

mismatch repair

type of repair mechanism in which mismatched bases are removed after replication

nucleotide excision repair

type of DNA repair mechanism in which the wrong base, along with a few nucleotides upstream or downstream, are removed

proofreading

function of DNA pol in which it reads the newly added base before adding the next one

point mutation

mutation that affects a single base

silent mutation

mutation that is not expressed

spontaneous mutation

mutation that takes place in the cells as a result of chemical reactions taking place naturally without exposure to any external agent

transition substitution

when a purine is replaced with a purine or a pyrimidine is replaced with another pyrimidine

transversion substitution

when a purine is replaced by a pyrimidine or a pyrimidine is replaced by a purine

Bis2A 11.3 Genome Sequencing

By the end of this section, you will be able to:

- Describe three types of sequencing
- Define whole-genome sequencing

Although there have been significant advances in the medical sciences in recent years, doctors are still confounded by some diseases, and they are using whole-genome sequencing to get to the bottom of the problem.

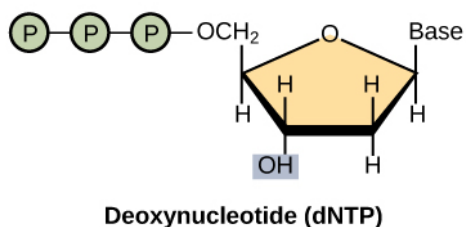
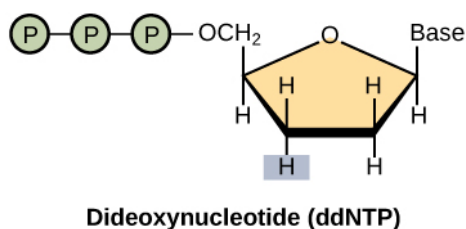
Whole-genome sequencing is a process that determines the DNA sequence of an entire genome. Whole-genome sequencing is a brute-force approach to problem solving when there is a genetic basis at the core of a disease. Several laboratories now provide services to sequence, analyze, and interpret entire genomes.

For example, whole-exome sequencing is a lower-cost alternative to whole genome sequencing. In exome sequencing, only the coding, exon-producing regions of the DNA are sequenced. In 2010, whole-exome sequencing was used to save a young boy whose intestines had multiple mysterious abscesses. The child had several colon operations with no relief. Finally, whole-exome sequencing was performed, which revealed a defect in a pathway that controls apoptosis (programmed cell death). A bone-marrow transplant was used to overcome this genetic disorder, leading to a cure for the boy. He was the first person to be successfully treated based on a diagnosis made by whole-exome sequencing. Today, human genome sequencing is more readily available and can be completed in a day or two for about \$1000.

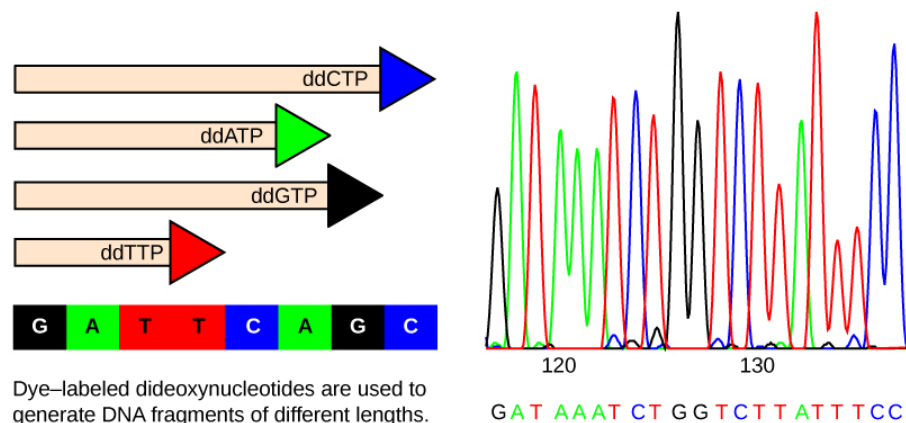
Strategies Used in Sequencing Projects

The basic sequencing technique used in all modern day sequencing projects is the chain termination method (also known as the dideoxy method), which was developed by Fred Sanger in the 1970s. The chain termination method involves DNA replication of a single-stranded template with the use of a primer and a regular **deoxynucleotide** (dNTP), which is a monomer, or a single unit, of DNA. The primer and dNTP are mixed with a small proportion of fluorescently labeled **dideoxynucleotides** (ddNTPs). The

ddNTPs are monomers that are missing a hydroxyl group (-OH) at the site at which another nucleotide usually attaches to form a chain ([\[link\]](#)). Each ddNTP is labeled with a different color of fluorophore. Every time a ddNTP is incorporated in the growing complementary strand, it terminates the process of DNA replication, which results in multiple short strands of replicated DNA that are each terminated at a different point during replication. When the reaction mixture is processed by gel electrophoresis after being separated into single strands, the multiple newly replicated DNA strands form a ladder because of the differing sizes. Because the ddNTPs are fluorescently labeled, each band on the gel reflects the size of the DNA strand and the ddNTP that terminated the reaction. The different colors of the fluorophore-labeled ddNTPs help identify the ddNTP incorporated at that position. Reading the gel on the basis of the color of each band on the ladder produces the sequence of the template strand ([\[link\]](#)).



A dideoxynucleotide is similar in structure to a deoxynucleotide, but is missing the 3' hydroxyl group (indicated by the box). When a dideoxynucleotide is incorporated into a DNA strand, DNA synthesis stops.



Frederick Sanger's dideoxy chain termination method is illustrated. Using dideoxynucleotides, the DNA fragment can be terminated at different points. The DNA is separated on the basis of size, and these bands, based on the size of the fragments, can be read.

Early Strategies: Shotgun Sequencing and Pair-Wise End Sequencing

In **shotgun sequencing** method, several copies of a DNA fragment are cut randomly into many smaller pieces (somewhat like what happens to a round shot cartridge when fired from a shotgun). All of the segments are then sequenced using the chain-sequencing method. Then, with the help of a computer, the fragments are analyzed to see where their sequences overlap. By matching up overlapping sequences at the end of each fragment, the entire DNA sequence can be reformed. A larger sequence that is assembled from overlapping shorter sequences is called a **contig**. As an analogy, consider that someone has four copies of a landscape photograph that you have never seen before and know nothing about how it should appear. The person then rips up each photograph with their hands, so that different size pieces are present from each copy. The person then mixes all of the pieces together and asks you to reconstruct the photograph. In one of the smaller pieces you see a mountain. In a larger piece, you see that the same mountain

is behind a lake. A third fragment shows only the lake, but it reveals that there is a cabin on the shore of the lake. Therefore, from looking at the overlapping information in these three fragments, you know that the picture contains a mountain behind a lake that has a cabin on its shore. This is the principle behind reconstructing entire DNA sequences using shotgun sequencing.

Originally, shotgun sequencing only analyzed one end of each fragment for overlaps. This was sufficient for sequencing small genomes. However, the desire to sequence larger genomes, such as that of a human, led to the development of double-barrel shotgun sequencing, more formally known as **pairwise-end sequencing**. In pairwise-end sequencing, both ends of each fragment are analyzed for overlap. Pairwise-end sequencing is, therefore, more cumbersome than shotgun sequencing, but it is easier to reconstruct the sequence because there is more available information.

Next-generation Sequencing

Since 2005, automated sequencing techniques used by laboratories are under the umbrella of **next-generation sequencing**, which is a group of automated techniques used for rapid DNA sequencing. These automated low-cost sequencers can generate sequences of hundreds of thousands or millions of short fragments (25 to 500 base pairs) in the span of one day. These sequencers use sophisticated software to get through the cumbersome process of putting all the fragments in order.

Note:

Evolution Connection

Comparing Sequences

A sequence alignment is an arrangement of proteins, DNA, or RNA; it is used to identify regions of similarity between cell types or species, which may indicate conservation of function or structures. Sequence alignments may be used to construct phylogenetic trees. The following website uses a software program called [BLAST \(basic local alignment search tool\)](#).

Under “Basic Blast,” click “Nucleotide Blast.” Input the following sequence into the large "query sequence" box: ATTGCTTCGATTGCA. Below the box, locate the "Species" field and type "human" or "Homo sapiens". Then click “BLAST” to compare the inputted sequence against known sequences of the human genome. The result is that this sequence occurs in over a hundred places in the human genome. Scroll down below the graphic with the horizontal bars and you will see short description of each of the matching hits. Pick one of the hits near the top of the list and click on "Graphics". This will bring you to a page that shows where the sequence is found within the entire human genome. You can move the slider that looks like a green flag back and forth to view the sequences immediately around the selected gene. You can then return to your selected sequence by clicking the "ATG" button.

Use of Whole-Genome Sequences of Model Organisms

The first genome to be completely sequenced was of a bacterial virus, the bacteriophage *φx174* (5368 base pairs); this was accomplished by Fred Sanger using shotgun sequencing. Several other organelle and viral genomes were later sequenced. The first organism whose genome was sequenced was the bacterium *Haemophilus influenzae*; this was accomplished by Craig Venter in the 1980s. Approximately 74 different laboratories collaborated on the sequencing of the genome of the yeast *Saccharomyces cerevisiae*, which began in 1989 and was completed in 1996, because it was 60 times bigger than any other genome that had been sequenced. By 1997, the genome sequences of two important model organisms were available: the bacterium *Escherichia coli* K12 and the yeast *Saccharomyces cerevisiae*. Genomes of other model organisms, such as the mouse *Mus musculus*, the fruit fly *Drosophila melanogaster*, the nematode *Caenorhabditis. elegans*, and humans *Homo sapiens* are now known. A lot of basic research is performed in model organisms because the information can be applied to genetically similar organisms. A **model organism** is a species that is studied as a model to understand the biological processes in other species represented by the model organism. Having entire genomes sequenced helps with the research efforts in these model organisms. The

process of attaching biological information to gene sequences is called **genome annotation**. Annotation of gene sequences helps with basic experiments in molecular biology, such as designing PCR primers and RNA targets.

Note:

Link to Learning



Click through each step of genome sequencing at this [site](#).

Uses of Genome Sequences

DNA microarrays are methods used to detect gene expression by analyzing an array of DNA fragments that are fixed to a glass slide or a silicon chip to identify active genes and identify sequences. Almost one million genotypic abnormalities can be discovered using microarrays, whereas whole-genome sequencing can provide information about all six billion base pairs in the human genome. Although the study of medical applications of genome sequencing is interesting, this discipline tends to dwell on abnormal gene function. Knowledge of the entire genome will allow future onset diseases and other genetic disorders to be discovered early, which will allow for more informed decisions to be made about lifestyle, medication, and having children. Genomics is still in its infancy, although someday it may become routine to use whole-genome sequencing to screen every newborn to detect genetic abnormalities.

In addition to disease and medicine, genomics can contribute to the development of novel enzymes that convert biomass to biofuel, which

results in higher crop and fuel production, and lower cost to the consumer. This knowledge should allow better methods of control over the microbes that are used in the production of biofuels. Genomics could also improve the methods used to monitor the impact of pollutants on ecosystems and help clean up environmental contaminants. Genomics has allowed for the development of agrochemicals and pharmaceuticals that could benefit medical science and agriculture.

It sounds great to have all the knowledge we can get from whole-genome sequencing; however, humans have a responsibility to use this knowledge wisely. Otherwise, it could be easy to misuse the power of such knowledge, leading to discrimination based on a person's genetics, human genetic engineering, and other ethical concerns. This information could also lead to legal issues regarding health and privacy.

Section Summary

Whole-genome sequencing is the latest available resource to treat genetic diseases. Some doctors are using whole-genome sequencing to save lives. Genomics has many industrial applications including biofuel development, agriculture, pharmaceuticals, and pollution control. The basic principle of all modern-day sequencing strategies involves the chain termination method of sequencing.

Although the human genome sequences provide key insights to medical professionals, researchers use whole-genome sequences of model organisms to better understand the genome of the species. Automation and the decreased cost of whole-genome sequencing may lead to personalized medicine in the future.

Review Questions

Exercise:

Problem: The chain termination method of sequencing:

- a. uses labeled ddNTPs
- b. uses only dideoxynucleotides
- c. uses only deoxynucleotides
- d. uses labeled dNTPs

Solution:

A

Exercise:

Problem: Whole-genome sequencing can be used for advances in:

- a. the medical field
- b. agriculture
- c. biofuels
- d. all of the above

Solution:

D

Exercise:

Problem: Sequencing an individual person's genome

- a. is currently possible
- b. could lead to legal issues regarding discrimination and privacy
- c. could help make informed choices about medical treatment
- d. all of the above

Solution:

D

Exercise:

Problem:

What is the most challenging issue facing genome sequencing?

- a. the inability to develop fast and accurate sequencing techniques
- b. the ethics of using information from genomes at the individual level
- c. the availability and stability of DNA
- d. all of the above

Solution:

B

Glossary

chain termination method

method of DNA sequencing using labeled dideoxynucleotides to terminate DNA replication; it is also called the dideoxy method or the Sanger method

contig

larger sequence of DNA assembled from overlapping shorter sequences

deoxynucleotide

individual monomer (single unit) of DNA

dideoxynucleotide

individual monomer of DNA that is missing a hydroxyl group (–OH)

DNA microarray

method used to detect gene expression by analyzing an array of DNA fragments that are fixed to a glass slide or a silicon chip to identify active genes and identify sequences

genome annotation

process of attaching biological information to gene sequences

model organism

species that is studied and used as a model to understand the biological processes in other species represented by the model organism

next-generation sequencing

group of automated techniques used for rapid DNA sequencing

shotgun sequencing

method used to sequence multiple DNA fragments to generate the sequence of a large piece of DNA

whole-genome sequencing

process that determines the DNA sequence of an entire genome

Bis2A 11.4 Manipulations of DNA and its uses in Biotechnology

By the end of this section, you will be able to:

- Explain the basic techniques used to manipulate genetic material
- Explain molecular and reproductive cloning

Biotechnology is the use of artificial methods to modify the genetic material of living organisms or cells to produce novel compounds or to perform new functions. Biotechnology has been used for improving livestock and crops since the beginning of agriculture through selective breeding. Since the discovery of the structure of DNA in 1953, and particularly since the development of tools and methods to manipulate DNA in the 1970s, biotechnology has become synonymous with the manipulation of organisms' DNA at the molecular level. The primary applications of this technology are in medicine (for the production of vaccines and antibiotics) and in agriculture (for the genetic modification of crops). Biotechnology also has many industrial applications, such as fermentation, the treatment of oil spills, and the production of biofuels, as well as many household applications such as the use of enzymes in laundry detergent.

Manipulating Genetic Material

To accomplish the applications described above, biotechnologists must be able to extract, manipulate, and analyze nucleic acids.

Review of Nucleic Acid Structure

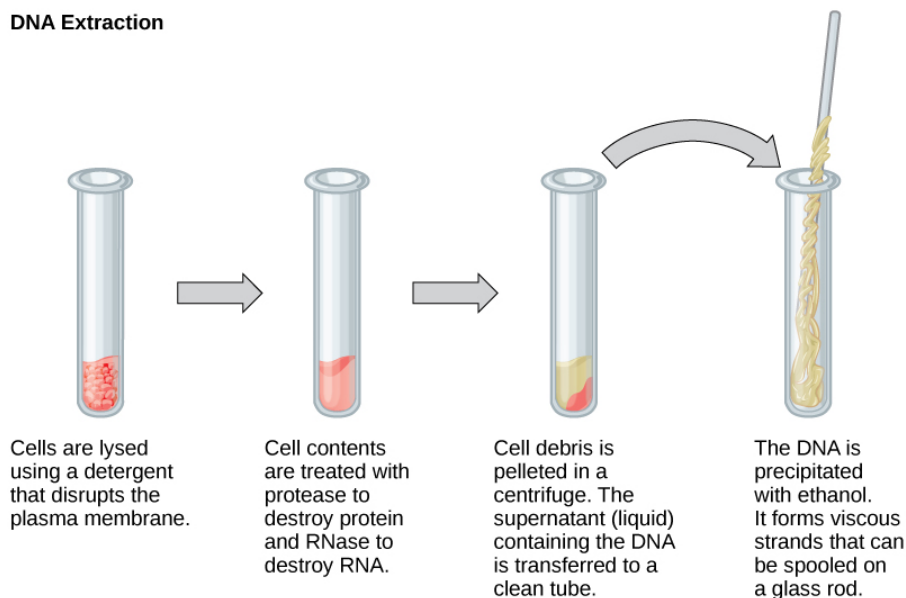
To understand the basic techniques used to work with nucleic acids, remember that nucleic acids are macromolecules made of nucleotides (a sugar, a phosphate, and a nitrogenous base). The phosphate groups on these molecules each have a net negative charge. An entire set of DNA molecules in the nucleus of eukaryotic organisms is called the genome. DNA has two complementary strands linked by hydrogen bonds between the paired bases.

Unlike DNA in eukaryotic cells, RNA molecules leave the nucleus. Messenger RNA (mRNA) is analyzed most frequently because it represents the protein-coding genes that are being expressed in the cell.

Isolation of Nucleic Acids

To study or manipulate nucleic acids, the DNA must first be extracted from cells. Various techniques are used to extract different types of DNA ([\[link\]](#)). Most nucleic acid extraction techniques involve steps to break open the cell, and then the use of enzymatic reactions to destroy all undesired macromolecules. Cells are broken open using a detergent solution containing buffering compounds. To prevent degradation and contamination, macromolecules such as proteins and RNA are inactivated using enzymes. The DNA is then brought out of solution using alcohol. The resulting DNA, because it is made up of long polymers, forms a gelatinous mass.

DNA Extraction

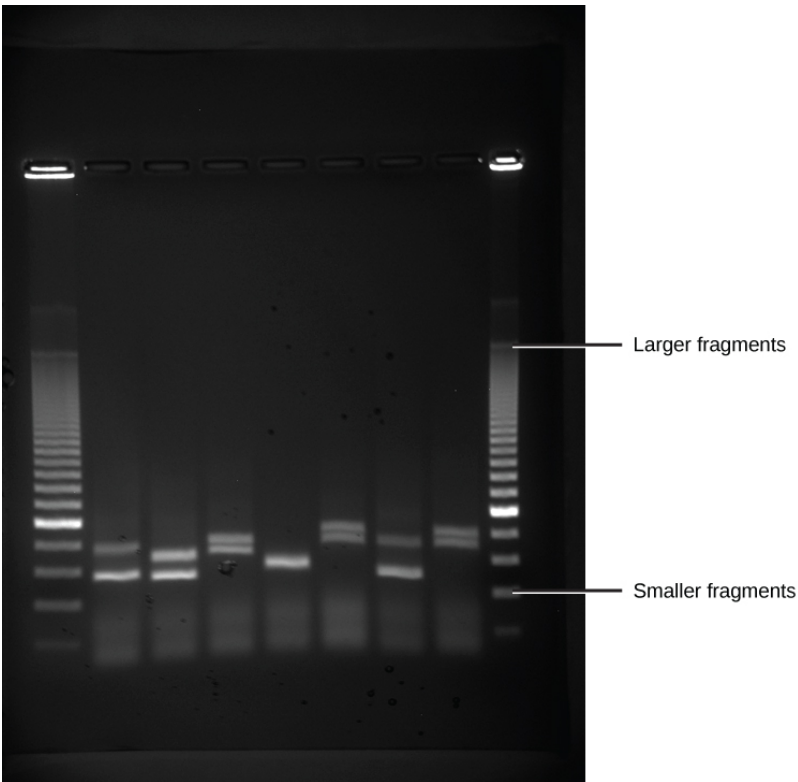


This diagram shows the basic method used for the extraction of DNA.

RNA is studied to understand gene expression patterns in cells. RNA is naturally very unstable because enzymes that break down RNA are commonly present in nature. Some are even secreted by our own skin and are very difficult to inactivate. Similar to DNA extraction, RNA extraction involves the use of various buffers and enzymes to inactivate other macromolecules and preserve only the RNA.

Gel Electrophoresis

Because nucleic acids are negatively charged ions at neutral or alkaline pH in an aqueous environment, they can be moved by an electric field. **Gel electrophoresis** is a technique used to separate charged molecules on the basis of size and charge. The nucleic acids can be separated as whole chromosomes or as fragments. The nucleic acids are loaded into a slot at one end of a gel matrix, an electric current is applied, and negatively charged molecules are pulled toward the opposite end of the gel (the end with the positive electrode). Smaller molecules move through the pores in the gel faster than larger molecules; this difference in the rate of migration separates the fragments on the basis of size. The nucleic acids in a gel matrix are invisible until they are stained with a compound that allows them to be seen, such as a dye. Distinct fragments of nucleic acids appear as bands at specific distances from the top of the gel (the negative electrode end) that are based on their size ([\[link\]](#)). A mixture of many fragments of varying sizes appear as a long smear, whereas uncut genomic DNA is usually too large to run through the gel and forms a single large band at the top of the gel.

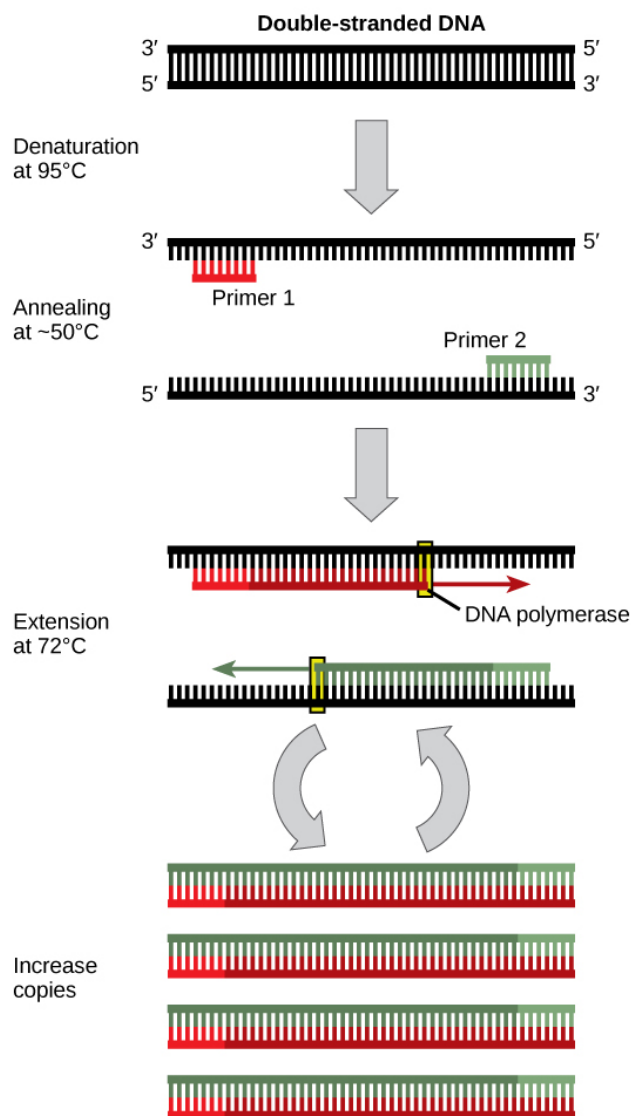


Shown are DNA fragments from six samples run on a gel, stained with a fluorescent dye and viewed under UV light. (credit: modification of work by James Jacob, Tompkins Cortland Community College)

Polymerase Chain Reaction

DNA analysis often requires focusing on one or more specific regions of the genome. It also frequently involves situations in which only one or a few copies of a DNA molecule are available for further analysis. These amounts are insufficient for most procedures, such as gel electrophoresis. **Polymerase chain reaction (PCR)** is a technique used to rapidly increase the number of copies of specific regions of DNA for further analyses ([link](#)). PCR uses a special form of DNA polymerase, the enzyme that

replicates DNA, and other short nucleotide sequences called primers that base pair to a specific portion of the DNA being replicated. PCR is used for many purposes in laboratories. These include: 1) the identification of the owner of a DNA sample left at a crime scene; 2) paternity analysis; 3) the comparison of small amounts of ancient DNA with modern organisms; and 4) determining the sequence of nucleotides in a specific region.



Polymerase chain reaction, or PCR, is used to produce many copies of a specific sequence of

DNA using a special form of DNA polymerase.

Cloning

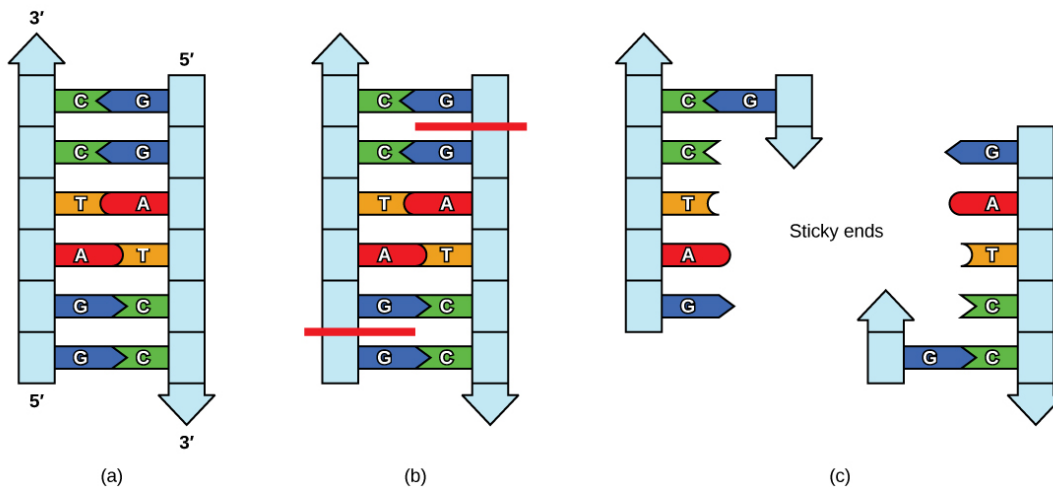
In general, **cloning** means the creation of a perfect replica. Typically, the word is used to describe the creation of a genetically identical copy. In biology, the re-creation of a whole organism is referred to as “reproductive cloning.” Long before attempts were made to clone an entire organism, researchers learned how to copy short stretches of DNA—a process that is referred to as molecular cloning.

Molecular Cloning

Cloning allows for the creation of multiple copies of genes, expression of genes, and study of specific genes. To get the DNA fragment into a bacterial cell in a form that will be copied or expressed, the fragment is first inserted into a plasmid. A **plasmid** (also called a vector in this context) is a small circular DNA molecule that replicates independently of the chromosomal DNA in bacteria. In cloning, the plasmid molecules can be used to provide a "vehicle" in which to insert a desired DNA fragment. Modified plasmids are usually reintroduced into a bacterial host for replication. As the bacteria divide, they copy their own DNA (including the plasmids). The inserted DNA fragment is copied along with the rest of the bacterial DNA. In a bacterial cell, the fragment of DNA from the human genome (or another organism that is being studied) is referred to as foreign DNA to differentiate it from the DNA of the bacterium (the host DNA).

Plasmids occur naturally in bacterial populations (such as *Escherichia coli*) and have genes that can contribute favorable traits to the organism, such as antibiotic resistance (the ability to be unaffected by antibiotics). Plasmids have been highly engineered as vectors for molecular cloning and for the subsequent large-scale production of important molecules, such as insulin.

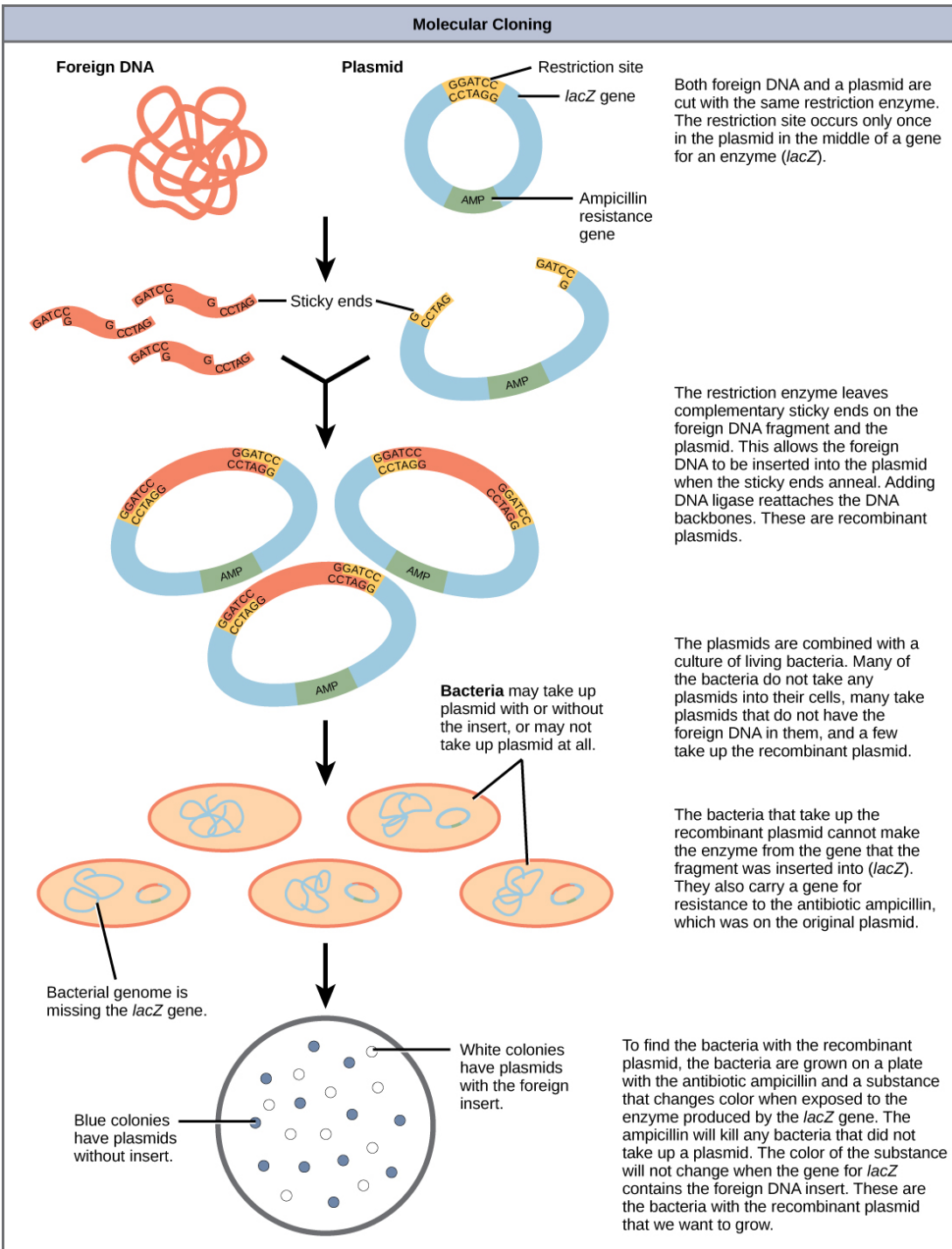
A valuable characteristic of plasmid vectors is the ease with which a foreign DNA fragment can be introduced. These plasmid vectors contain many short DNA sequences that can be cut with different commonly available **restriction enzymes**. Restriction enzymes (also called restriction endonucleases) recognize specific DNA sequences and cut them in a predictable manner; they are naturally produced by bacteria as a defense mechanism against foreign DNA. Many restriction enzymes make staggered cuts in the two strands of DNA, such that the cut ends have a 2- to 4-nucleotide single-stranded overhang. The sequence that is recognized by the restriction enzyme is a four- to eight-nucleotide sequence that is a palindrome. Like with a word palindrome, this means the sequence reads the same forward and backward. In most cases, the sequence reads the same forward on one strand and backward on the complementary strand. When a staggered cut is made in a sequence like this, the overhangs are complementary ([link](#)).



In this (a) six-nucleotide restriction enzyme recognition site, notice that the sequence of six nucleotides reads the same in the 5' to 3' direction on one strand as it does in the 5' to 3' direction on the complementary strand. This is known as a palindrome. (b) The restriction enzyme makes breaks in the DNA strands, and (c) the cut in the DNA results in “sticky ends”. Another piece of DNA cut on either end by the same

restriction enzyme could attach to these sticky ends and be inserted into the gap made by this cut.

Because these overhangs are capable of coming back together by hydrogen bonding with complementary overhangs on a piece of DNA cut with the same restriction enzyme, these are called “sticky ends.” The process of forming hydrogen bonds between complementary sequences on single strands to form double-stranded DNA is called **annealing**. Addition of an enzyme called DNA ligase, which takes part in DNA replication in cells, permanently joins the DNA fragments when the sticky ends come together. In this way, any DNA fragment can be spliced between the two ends of a plasmid DNA that has been cut with the same restriction enzyme ([link](#)).



This diagram shows the steps involved in molecular cloning.

Plasmids with foreign DNA inserted into them are called **recombinant DNA** molecules because they contain new combinations of genetic material. Proteins that are produced from recombinant DNA molecules are called **recombinant proteins**. Not all recombinant plasmids are capable of expressing genes. Plasmids may also be engineered to express proteins only when stimulated by certain environmental factors, so that scientists can control the expression of the recombinant proteins.

Genetic Engineering

Using recombinant DNA technology to modify an organism's DNA to achieve desirable traits is called **genetic engineering**. Addition of foreign DNA in the form of recombinant DNA vectors that are generated by molecular cloning is the most common method of genetic engineering. An organism that receives the recombinant DNA is called a **genetically modified organism** (GMO). If the foreign DNA that is introduced comes from a different species, the host organism is called **transgenic**. Bacteria, plants, and animals have been genetically modified since the early 1970s for academic, medical, agricultural, and industrial purposes. These applications will be examined in more detail in the next module.

Note:

Concept in Action



Watch this [short video](#) explaining how scientists create a transgenic animal.

Although the classic methods of studying the function of genes began with a given phenotype and determined the genetic basis of that phenotype, modern techniques allow researchers to start at the DNA sequence level and ask: "What does this gene or DNA element do?" This technique, called **reverse genetics**, has resulted in reversing the classical genetic methodology. One example of this method is analogous to damaging a body part to determine its function. An insect that loses a wing cannot fly, which means that the wing's function is flight. The classic genetic method compares insects that cannot fly with insects that can fly, and observes that the non-flying insects have lost wings. Similarly in a reverse genetics approach, mutating or deleting genes provides researchers with clues about gene function. Alternately, reverse genetics can be used to cause a gene to overexpress itself to determine what phenotypic effects may occur.

Section Summary

Nucleic acids can be isolated from cells for the purposes of further analysis by breaking open the cells and enzymatically destroying all other major macromolecules. Fragmented or whole chromosomes can be separated on the basis of size by gel electrophoresis. Short stretches of DNA can be amplified by PCR. DNA can be cut (and subsequently re-spliced together) using restriction enzymes. The molecular and cellular techniques of biotechnology allow researchers to genetically engineer organisms, modifying them to achieve desirable traits.

Cloning may involve cloning small DNA fragments (molecular cloning), or cloning entire organisms (reproductive cloning). In molecular cloning with bacteria, a desired DNA fragment is inserted into a bacterial plasmid using restriction enzymes and the plasmid is taken up by a bacterium, which will then express the foreign DNA. Using other techniques, foreign genes can be inserted into eukaryotic organisms. In each case, the organisms are called transgenic organisms. In reproductive cloning, a donor nucleus is put into an enucleated egg cell, which is then stimulated to divide and develop into an organism.

In reverse genetics methods, a gene is mutated or removed in some way to identify its effect on the phenotype of the whole organism as a way to

determine its function.

Art Connections

Exercise:

Problem:

[\[link\]](#) Why was Dolly a Finn-Dorset and not a Scottish Blackface sheep?

Solution:

[\[link\]](#) Because even though the original cell came from a Scottish Blackface sheep and the surrogate mother was a Scottish Blackface, the DNA came from a Finn-Dorset.

Glossary

anneal

in molecular biology, the process by which two single strands of DNA hydrogen bond at complementary nucleotides to form a double-stranded molecule

biotechnology

the use of artificial methods to modify the genetic material of living organisms or cells to produce novel compounds or to perform new functions

cloning

the production of an exact copy—specifically, an exact genetic copy—of a gene, cell, or organism

gel electrophoresis

a technique used to separate molecules on the basis of their ability to migrate through a semisolid gel in response to an electric current

genetic engineering

alteration of the genetic makeup of an organism using the molecular methods of biotechnology

genetically modified organism (GMO)

an organism whose genome has been artificially changed

plasmid

a small circular molecule of DNA found in bacteria that replicates independently of the main bacterial chromosome; plasmids code for some important traits for bacteria and can be used as vectors to transport DNA into bacteria in genetic engineering applications

polymerase chain reaction (PCR)

a technique used to make multiple copies of DNA

recombinant DNA

a combination of DNA fragments generated by molecular cloning that does not exist in nature

recombinant protein

a protein that is expressed from recombinant DNA molecules

restriction enzyme

an enzyme that recognizes a specific nucleotide sequence in DNA and cuts the DNA double strand at that recognition site, often with a staggered cut leaving short single strands or “sticky” ends

reverse genetics

a form of genetic analysis that manipulates DNA to disrupt or affect the product of a gene to analyze the gene’s function

reproductive cloning

cloning of entire organisms

transgenic

describing an organism that receives DNA from a different species

Bis2A 12.0 Transcription

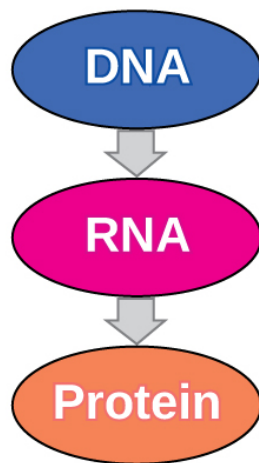
By the end of this section, you will be able to:

- Explain the central dogma
- Explain the main steps of transcription
- Describe how eukaryotic mRNA is processed

In both prokaryotes and eukaryotes, the second function of DNA (the first was replication) is to provide the information needed to construct the proteins necessary so that the cell can perform all of its functions. To do this, the DNA is “read” or transcribed into an **mRNA** molecule. The mRNA then provides the code to form a protein by a process called translation. Through the processes of transcription and translation, a protein is built with a specific sequence of amino acids that was originally encoded in the DNA. This module discusses the details of transcription.

The Central Dogma: DNA Encodes RNA; RNA Encodes Protein

The flow of genetic information in cells from DNA to mRNA to protein is described by the central dogma ([\[link\]](#)), which states that genes specify the sequences of mRNAs, which in turn specify the sequences of proteins.



The central dogma states that

DNA encodes RNA, which in turn
encodes protein.

The copying of DNA to mRNA is relatively straightforward, with one nucleotide being added to the mRNA strand for every complementary nucleotide read in the DNA strand. The translation to protein is more complex because groups of three mRNA nucleotides correspond to one amino acid of the protein sequence. However, as we shall see in the next module, the translation to protein is still systematic, such that nucleotides 1 to 3 correspond to amino acid 1, nucleotides 4 to 6 correspond to amino acid 2, and so on.

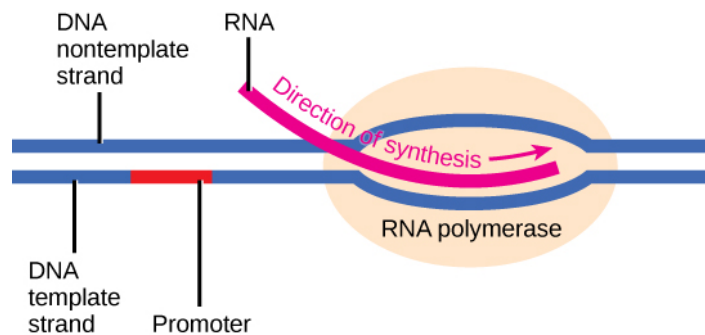
Transcription: from DNA to mRNA

Both prokaryotes and eukaryotes perform fundamentally the same process of transcription, with the important difference of the membrane-bound nucleus in eukaryotes. With the genes bound in the nucleus, transcription occurs in the nucleus of the cell and the mRNA transcript must be transported to the cytoplasm. The prokaryotes, which include bacteria and archaea, lack membrane-bound nuclei and other organelles, and transcription occurs in the cytoplasm of the cell. In both prokaryotes and eukaryotes, transcription occurs in three main stages: initiation, elongation, and termination.

Initiation

Transcription requires the DNA double helix to partially unwind in the region of mRNA synthesis. The region of unwinding is called a **transcription bubble**. The DNA sequence onto which the proteins and enzymes involved in transcription bind to initiate the process is called a **promoter**. In most cases, promoters exist upstream of the genes they regulate. The specific sequence of a promoter is very important because it

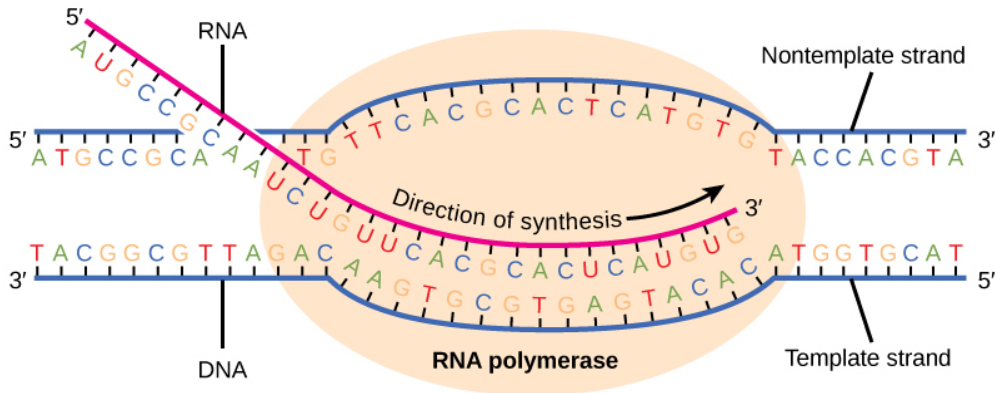
determines whether the corresponding gene is transcribed all of the time, some of the time, or hardly at all ([\[link\]](#)).



The initiation of transcription begins when DNA is unwound, forming a transcription bubble. Enzymes and other proteins involved in transcription bind at the promoter.

Elongation

Transcription always proceeds from one of the two DNA strands, which is called the **template strand**. The mRNA product is complementary to the template strand and is almost identical to the other DNA strand, called the **nontemplate strand**, with the exception that RNA contains a uracil (U) in place of the thymine (T) found in DNA. During elongation, an enzyme called **RNA polymerase** proceeds along the DNA template adding nucleotides by base pairing with the DNA template in a manner similar to DNA replication, with the difference that an RNA strand is being synthesized that does not remain bound to the DNA template. As elongation proceeds, the DNA is continuously unwound ahead of the core enzyme and rewound behind it ([\[link\]](#)).

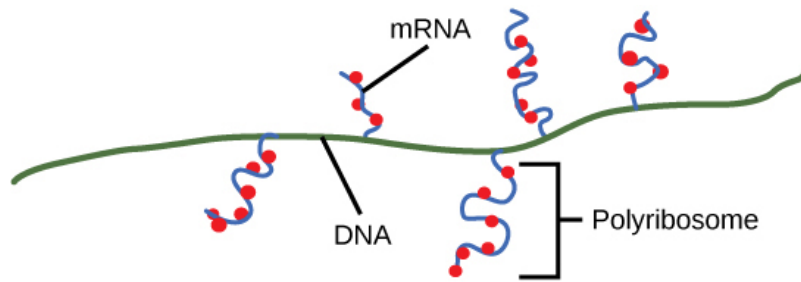


During elongation, RNA polymerase tracks along the DNA template, synthesizes mRNA in the 5' to 3' direction, and unwinds then rewinds the DNA as it is read.

Termination

Once a gene is transcribed, the prokaryotic polymerase needs to be instructed to dissociate from the DNA template and liberate the newly made mRNA. Depending on the gene being transcribed, there are two kinds of termination signals, but both involve repeated nucleotide sequences in the DNA template that result in RNA polymerase stalling, leaving the DNA template, and freeing the mRNA transcript.

On termination, the process of transcription is complete. In a prokaryotic cell, by the time termination occurs, the transcript would already have been used to partially synthesize numerous copies of the encoded protein because these processes can occur concurrently using multiple ribosomes (polyribosomes) ([link](#)). In contrast, the presence of a nucleus in eukaryotic cells precludes simultaneous transcription and translation.



Multiple polymerases can transcribe a single bacterial gene while numerous ribosomes concurrently translate the mRNA transcripts into polypeptides. In this way, a specific protein can rapidly reach a high concentration in the bacterial cell.

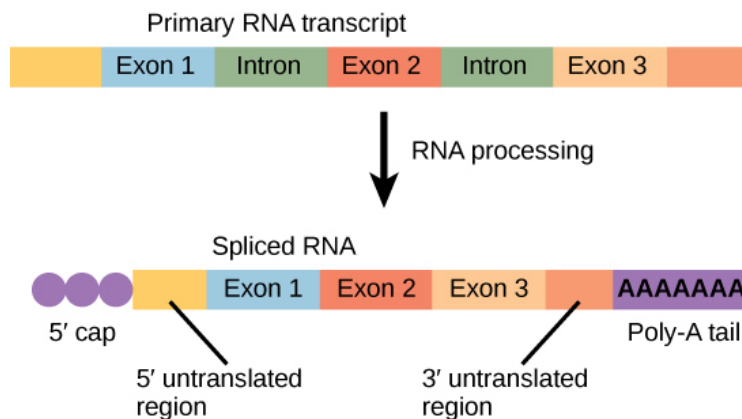
Eukaryotic RNA Processing

The newly transcribed eukaryotic mRNAs must undergo several processing steps before they can be transferred from the nucleus to the cytoplasm and translated into a protein. The additional steps involved in eukaryotic mRNA maturation create a molecule that is much more stable than a prokaryotic mRNA. For example, eukaryotic mRNAs last for several hours, whereas the typical prokaryotic mRNA lasts no more than five seconds.

The mRNA transcript is first coated in RNA-stabilizing proteins to prevent it from degrading while it is processed and exported out of the nucleus. This occurs while the pre-mRNA still is being synthesized by adding a special nucleotide “cap” to the 5' end of the growing transcript. In addition to preventing degradation, factors involved in protein synthesis recognize the cap to help initiate translation by ribosomes.

Once elongation is complete, an enzyme then adds a string of approximately 200 adenine residues to the 3' end, called the poly-A tail. This modification further protects the pre-mRNA from degradation and signals to cellular factors that the transcript needs to be exported to the cytoplasm.

Eukaryotic genes are composed of protein-coding sequences called **exons** (*ex-on* signifies that they are *expressed*) and *intervening* sequences called **introns** (*int-ron* denotes their *intervening* role). Introns are removed from the pre-mRNA during processing. Intron sequences in mRNA do not encode functional proteins. It is essential that all of a pre-mRNA's introns be completely and precisely removed before protein synthesis so that the exons join together to code for the correct amino acids. If the process errs by even a single nucleotide, the sequence of the rejoined exons would be shifted, and the resulting protein would be nonfunctional. The process of removing introns and reconnecting exons is called **splicing** ([\[link\]](#)). Introns are removed and degraded while the pre-mRNA is still in the nucleus.



Eukaryotic mRNA contains introns that must be spliced out. A 5' cap and 3' tail are also added.

Section Summary

In prokaryotes, mRNA synthesis is initiated at a promoter sequence on the DNA template. Elongation synthesizes new mRNA. Termination liberates the mRNA and occurs by mechanisms that stall the RNA polymerase and cause it to fall off the DNA template. Newly transcribed eukaryotic mRNAs are modified with a cap and a poly-A tail. These structures protect the

mature mRNA from degradation and help export it from the nucleus. Eukaryotic mRNAs also undergo splicing, in which introns are removed and exons are reconnected with single-nucleotide accuracy. Only finished mRNAs are exported from the nucleus to the cytoplasm.

Multiple Choice

Exercise:

Problem: A promoter is _____.

- a. a specific sequence of DNA nucleotides
- b. a specific sequence of RNA nucleotides
- c. a protein that binds to DNA
- d. an enzyme that synthesizes RNA

Solution:

A

Exercise:

Problem:

Portions of eukaryotic mRNA sequence that are removed during RNA processing are _____.

- a. exons
- b. caps
- c. poly-A tails
- d. introns

Solution:

D

Glossary

exon

a sequence present in protein-coding mRNA after completion of pre-mRNA splicing

intron

non-protein-coding intervening sequences that are spliced from mRNA during processing

mRNA

messenger RNA; a form of RNA that carries the nucleotide sequence code for a protein sequence that is translated into a polypeptide sequence

nontemplate strand

the strand of DNA that is not used to transcribe mRNA; this strand is identical to the mRNA except that T nucleotides in the DNA are replaced by U nucleotides in the mRNA

promoter

a sequence on DNA to which RNA polymerase and associated factors bind and initiate transcription

RNA polymerase

an enzyme that synthesizes an RNA strand from a DNA template strand

splicing

the process of removing introns and reconnecting exons in a pre-mRNA

template strand

the strand of DNA that specifies the complementary mRNA molecule

transcription bubble

the region of locally unwound DNA that allows for transcription of mRNA

Bis2A 12.1 Bacterial Transcription

By the end of this section, you will be able to:

- List the different steps in prokaryotic transcription
- Discuss the role of promoters in prokaryotic transcription
- Describe how and when transcription is terminated

The prokaryotes, which include bacteria and archaea, are mostly single-celled organisms that, by definition, lack membrane-bound nuclei and other organelles. A bacterial chromosome is a covalently closed circle that, unlike eukaryotic chromosomes, is not organized around histone proteins. The central region of the cell in which prokaryotic DNA resides is called the nucleoid. In addition, prokaryotes often have abundant **plasmids**, which are shorter circular DNA molecules that may only contain one or a few genes. Plasmids can be transferred independently of the bacterial chromosome during cell division and often carry traits such as antibiotic resistance.

Transcription in prokaryotes (and in eukaryotes) requires the DNA double helix to partially unwind in the region of mRNA synthesis. The region of unwinding is called a **transcription bubble**. Transcription always proceeds from the same DNA strand for each gene, which is called the **template strand**. The mRNA product is complementary to the template strand and is almost identical to the other DNA strand, called the **nontemplate strand**. The only difference is that in mRNA, all of the T nucleotides are replaced with U nucleotides. In an RNA double helix, A can bind U via two hydrogen bonds, just as in A–T pairing in a DNA double helix.

The nucleotide pair in the DNA double helix that corresponds to the site from which the first 5' mRNA nucleotide is transcribed is called the +1 site, or the **initiation site**. Nucleotides preceding the initiation site are given negative numbers and are designated **upstream**. Conversely, nucleotides following the initiation site are denoted with “+” numbering and are called **downstream** nucleotides.

Initiation of Transcription in Prokaryotes

Prokaryotes do not have membrane-enclosed nuclei. Therefore, the processes of transcription, translation, and mRNA degradation can all occur simultaneously. The intracellular level of a bacterial protein can quickly be amplified by multiple transcription and translation events occurring concurrently on the same DNA template. Prokaryotic transcription often covers more than one gene and produces polycistronic mRNAs that specify more than one protein.

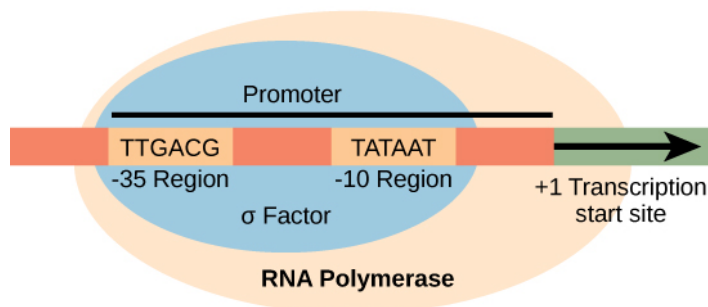
Our discussion here will exemplify transcription by describing this process in *Escherichia coli*, a well-studied bacterial species. Although some differences exist between transcription in *E. coli* and transcription in archaea, an understanding of *E. coli* transcription can be applied to virtually all bacterial species.

Prokaryotic RNA Polymerase

Prokaryotes use the same RNA polymerase to transcribe all of their genes. In *E. coli*, the polymerase is composed of five polypeptide subunits, two of which are identical. Four of these subunits, denoted α , α , β , and β' comprise the polymerase **core enzyme**. These subunits assemble every time a gene is transcribed, and they disassemble once transcription is complete. Each subunit has a unique role; the two α -subunits are necessary to assemble the polymerase on the DNA; the β -subunit binds to the ribonucleoside triphosphate that will become part of the nascent “recently born” mRNA molecule; and the β' binds the DNA template strand. The fifth subunit, σ , is involved only in transcription initiation. It confers transcriptional specificity such that the polymerase begins to synthesize mRNA from an appropriate initiation site. Without σ , the core enzyme would transcribe from random sites and would produce mRNA molecules that specified protein gibberish. The polymerase comprised of all five subunits is called the **holoenzyme**.

Prokaryotic Promoters

A **promoter** is a DNA sequence onto which the transcription machinery binds and initiates transcription. In most cases, promoters exist upstream of the genes they regulate. The specific sequence of a promoter is very important because it determines whether the corresponding gene is transcribed all the time, some of the time, or infrequently. Although promoters vary among prokaryotic genomes, a few elements are conserved. At the -10 and -35 regions upstream of the initiation site, there are two promoter **consensus** sequences, or regions that are similar across all promoters and across various bacterial species ([\[link\]](#)). The -10 consensus sequence, called the -10 region, is TATAAT. The -35 sequence, TTGACA, is recognized and bound by σ . Once this interaction is made, the subunits of the core enzyme bind to the site. The A–T-rich -10 region facilitates unwinding of the DNA template, and several phosphodiester bonds are made. The transcription initiation phase ends with the production of abortive transcripts, which are polymers of approximately 10 nucleotides that are made and released.



The σ subunit of prokaryotic RNA polymerase recognizes consensus sequences found in the promoter region upstream of the transcription start sight. The σ subunit dissociates from the polymerase after transcription has been initiated.

Note:

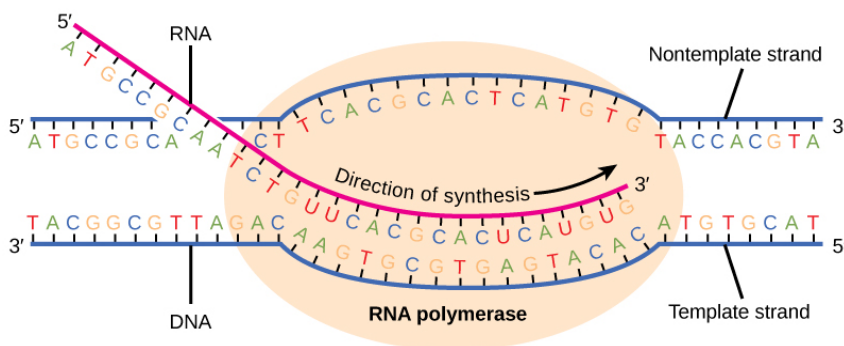
Link to Learning



View this [MolecularMovies animation](#) to see the first part of transcription and the base sequence repetition of the TATA box.

Elongation and Termination in Prokaryotes

The transcription elongation phase begins with the release of the σ subunit from the polymerase. The dissociation of σ allows the core enzyme to proceed along the DNA template, synthesizing mRNA in the 5' to 3' direction at a rate of approximately 40 nucleotides per second. As elongation proceeds, the DNA is continuously unwound ahead of the core enzyme and rewound behind it ([link](#)). The base pairing between DNA and RNA is not stable enough to maintain the stability of the mRNA synthesis components. Instead, the RNA polymerase acts as a stable linker between the DNA template and the nascent RNA strands to ensure that elongation is not interrupted prematurely.



During elongation, the prokaryotic RNA polymerase tracks along the DNA template, synthesizes mRNA in the 5' to 3' direction, and unwinds and rewinds the DNA as it is read.

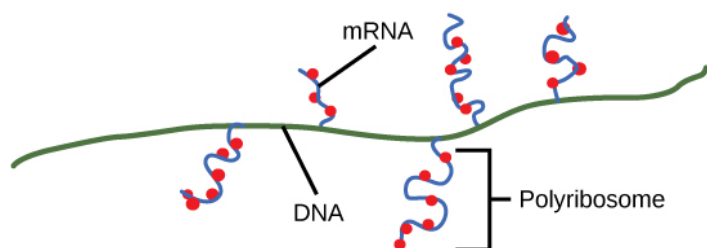
Prokaryotic Termination Signals

Once a gene is transcribed, the prokaryotic polymerase needs to be instructed to dissociate from the DNA template and liberate the newly made mRNA. Depending on the gene being transcribed, there are two kinds of termination signals. One is protein-based and the other is RNA-based. **Rho-dependent termination** is controlled by the rho protein, which tracks along behind the polymerase on the growing mRNA chain. Near the end of the gene, the polymerase encounters a run of G nucleotides on the DNA template and it stalls. As a result, the rho protein collides with the polymerase. The interaction with rho releases the mRNA from the transcription bubble.

Rho-independent termination is controlled by specific sequences in the DNA template strand. As the polymerase nears the end of the gene being transcribed, it encounters a region rich in C–G nucleotides. The mRNA folds back on itself, and the complementary C–G nucleotides bind together. The result is a stable **hairpin** that causes the polymerase to stall as soon as it begins to transcribe a region rich in A–T nucleotides. The complementary U–A region of the mRNA transcript forms only a weak interaction with the template DNA. This, coupled with the stalled polymerase, induces enough instability for the core enzyme to break away and liberate the new mRNA transcript.

Upon termination, the process of transcription is complete. By the time termination occurs, the prokaryotic transcript would already have been used to begin synthesis of numerous copies of the encoded protein because these processes can occur concurrently. The unification of transcription, translation, and even mRNA degradation is possible because all of these processes occur in the same 5' to 3' direction, and because there is no

membranous compartmentalization in the prokaryotic cell ([\[link\]](#)). In contrast, the presence of a nucleus in eukaryotic cells precludes simultaneous transcription and translation.



Multiple polymerases can transcribe a single bacterial gene while numerous ribosomes concurrently translate the mRNA transcripts into polypeptides.

In this way, a specific protein can rapidly reach a high concentration in the bacterial cell.

Note:

Link to Learning



Visit this [BioStudio animation](#) to see the process of prokaryotic transcription.

Section Summary

In prokaryotes, mRNA synthesis is initiated at a promoter sequence on the DNA template comprising two consensus sequences that recruit RNA polymerase. The prokaryotic polymerase consists of a core enzyme of four protein subunits and a σ protein that assists only with initiation. Elongation synthesizes mRNA in the 5' to 3' direction at a rate of 40 nucleotides per second. Termination liberates the mRNA and occurs either by rho protein interaction or by the formation of an mRNA hairpin.

Review Questions

Exercise:

Problem:

Which subunit of the *E. coli* polymerase confers specificity to transcription?

- a. α
- b. β
- c. β'
- d. σ

Solution:

D

Exercise:

Problem:

The -10 and -35 regions of prokaryotic promoters are called consensus sequences because _____.

- a. they are identical in all bacterial species
- b. they are similar in all bacterial species
- c. they exist in all organisms

d. they have the same function in all organisms

Solution:

B

Free Response

Exercise:

Problem:

If mRNA is complementary to the DNA template strand and the DNA template strand is complementary to the DNA nontemplate strand, then why are base sequences of mRNA and the DNA nontemplate strand not identical? Could they ever be?

Solution:

DNA is different from RNA in that T nucleotides in DNA are replaced with U nucleotides in RNA. Therefore, they could never be identical in base sequence.

Exercise:

Problem:

In your own words, describe the difference between rho-dependent and rho-independent termination of transcription in prokaryotes.

Solution:

Rho-dependent termination is controlled by the rho protein, which tracks along behind the polymerase on the growing mRNA chain. Near the end of the gene, the polymerase stalls at a run of G nucleotides on the DNA template. The rho protein collides with the polymerase and releases mRNA from the transcription bubble. Rho-independent termination is controlled by specific sequences in the DNA template

strand. As the polymerase nears the end of the gene being transcribed, it encounters a region rich in C–G nucleotides. This creates an mRNA hairpin that causes the polymerase to stall right as it begins to transcribe a region rich in A–T nucleotides. Because A–U bonds are less thermostable, the core enzyme falls away.

Glossary

consensus

DNA sequence that is used by many species to perform the same or similar functions

core enzyme

prokaryotic RNA polymerase consisting of α , α , β , and β' but missing σ ; this complex performs elongation

downstream

nucleotides following the initiation site in the direction of mRNA transcription; in general, sequences that are toward the 3' end relative to a site on the mRNA

hairpin

structure of RNA when it folds back on itself and forms intramolecular hydrogen bonds between complementary nucleotides

holoenzyme

prokaryotic RNA polymerase consisting of α , α , β , β' , and σ ; this complex is responsible for transcription initiation

initiation site

nucleotide from which mRNA synthesis proceeds in the 5' to 3' direction; denoted with a “+1”

nontemplate strand

strand of DNA that is not used to transcribe mRNA; this strand is identical to the mRNA except that T nucleotides in the DNA are replaced by U nucleotides in the mRNA

plasmid

extrachromosomal, covalently closed, circular DNA molecule that may only contain one or a few genes; common in prokaryotes

promoter

DNA sequence to which RNA polymerase and associated factors bind and initiate transcription

Rho-dependent termination

in prokaryotes, termination of transcription by an interaction between RNA polymerase and the rho protein at a run of G nucleotides on the DNA template

Rho-independent

termination sequence-dependent termination of prokaryotic mRNA synthesis; caused by hairpin formation in the mRNA that stalls the polymerase

TATA box

conserved promoter sequence in eukaryotes and prokaryotes that helps to establish the initiation site for transcription

template strand

strand of DNA that specifies the complementary mRNA molecule

transcription bubble

region of locally unwound DNA that allows for transcription of mRNA

upstream

nucleotides preceding the initiation site; in general, sequences toward the 5' end relative to a site on the mRNA

Bis2A 12.2 Eukaryotic Transcription

By the end of this section, you will be able to:

- List the steps in eukaryotic transcription
- Discuss the role of RNA polymerases in transcription
- Compare and contrast the three RNA polymerases
- Explain the significance of transcription factors

Prokaryotes and eukaryotes perform fundamentally the same process of transcription, with a few key differences. The most important difference between prokaryotes and eukaryotes is the latter's membrane-bound nucleus and organelles. With the genes bound in a nucleus, the eukaryotic cell must be able to transport its mRNA to the cytoplasm and must protect its mRNA from degrading before it is translated. Eukaryotes also employ three different polymerases that each transcribe a different subset of genes. Eukaryotic mRNAs are usually monogenic, meaning that they specify a single protein.

Initiation of Transcription in Eukaryotes

Unlike the prokaryotic polymerase that can bind to a DNA template on its own, eukaryotes require several other proteins, called transcription factors, to first bind to the promoter region and then help recruit the appropriate polymerase.

The Three Eukaryotic RNA Polymerases

The features of eukaryotic mRNA synthesis are markedly more complex those of prokaryotes. Instead of a single polymerase comprising five subunits, the eukaryotes have three polymerases that are each made up of 10 subunits or more. Each eukaryotic polymerase also requires a distinct set of transcription factors to bring it to the DNA template.

RNA polymerase I is located in the nucleolus, a specialized nuclear substructure in which ribosomal RNA (rRNA) is transcribed, processed, and assembled into ribosomes ([\[link\]](#)). The rRNA molecules are considered

structural RNAs because they have a cellular role but are not translated into protein. The rRNAs are components of the ribosome and are essential to the process of translation. RNA polymerase I synthesizes all of the rRNAs except for the 5S rRNA molecule. The “S” designation applies to “Svedberg” units, a nonadditive value that characterizes the speed at which a particle sediments during centrifugation.

Locations, Products, and Sensitivities of the Three Eukaryotic RNA Polymerases			
RNA Polymerase	Cellular Compartment	Product of Transcription	α-Amanitin Sensitivity
I	Nucleolus	All rRNAs except 5S rRNA	Insensitive
II	Nucleus	All protein-coding nuclear pre-mRNAs	Extremely sensitive
III	Nucleus	5S rRNA, tRNAs, and small nuclear RNAs	Moderately sensitive

RNA polymerase II is located in the nucleus and synthesizes all protein-coding nuclear pre-mRNAs. Eukaryotic pre-mRNAs undergo extensive processing after transcription but before translation. For clarity, this module’s discussion of transcription and translation in eukaryotes will use the term “mRNAs” to describe only the mature, processed molecules that

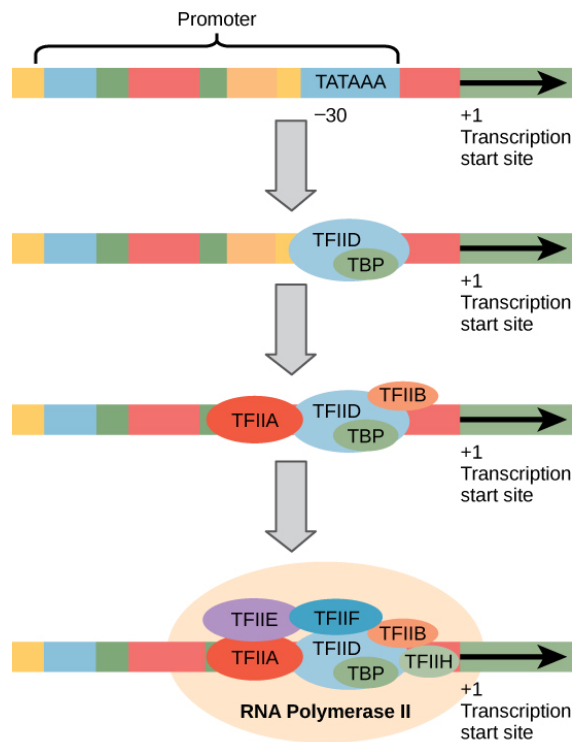
are ready to be translated. RNA polymerase II is responsible for transcribing the overwhelming majority of eukaryotic genes.

RNA polymerase III is also located in the nucleus. This polymerase transcribes a variety of structural RNAs that includes the 5S pre-rRNA, transfer pre-RNAs (pre-tRNAs), and **small nuclear pre-RNAs**. The tRNAs have a critical role in translation; they serve as the adaptor molecules between the mRNA template and the growing polypeptide chain. Small nuclear RNAs have a variety of functions, including “splicing” pre-mRNAs and regulating transcription factors.

A scientist characterizing a new gene can determine which polymerase transcribes it by testing whether the gene is expressed in the presence of a particular mushroom poison, α -amanitin ([\[link\]](#)). Interestingly, α -amanitin produced by *Amanita phalloides*, the Death Cap mushroom, affects the three polymerases very differently. RNA polymerase I is completely insensitive to α -amanitin, meaning that the polymerase can transcribe DNA in vitro in the presence of this poison. In contrast, RNA polymerase II is extremely sensitive to α -amanitin, and RNA polymerase III is moderately sensitive. Knowing the transcribing polymerase can clue a researcher into the general function of the gene being studied. Because RNA polymerase II transcribes the vast majority of genes, we will focus on this polymerase in our subsequent discussions about eukaryotic transcription factors and promoters.

Structure of an RNA Polymerase II Promoter

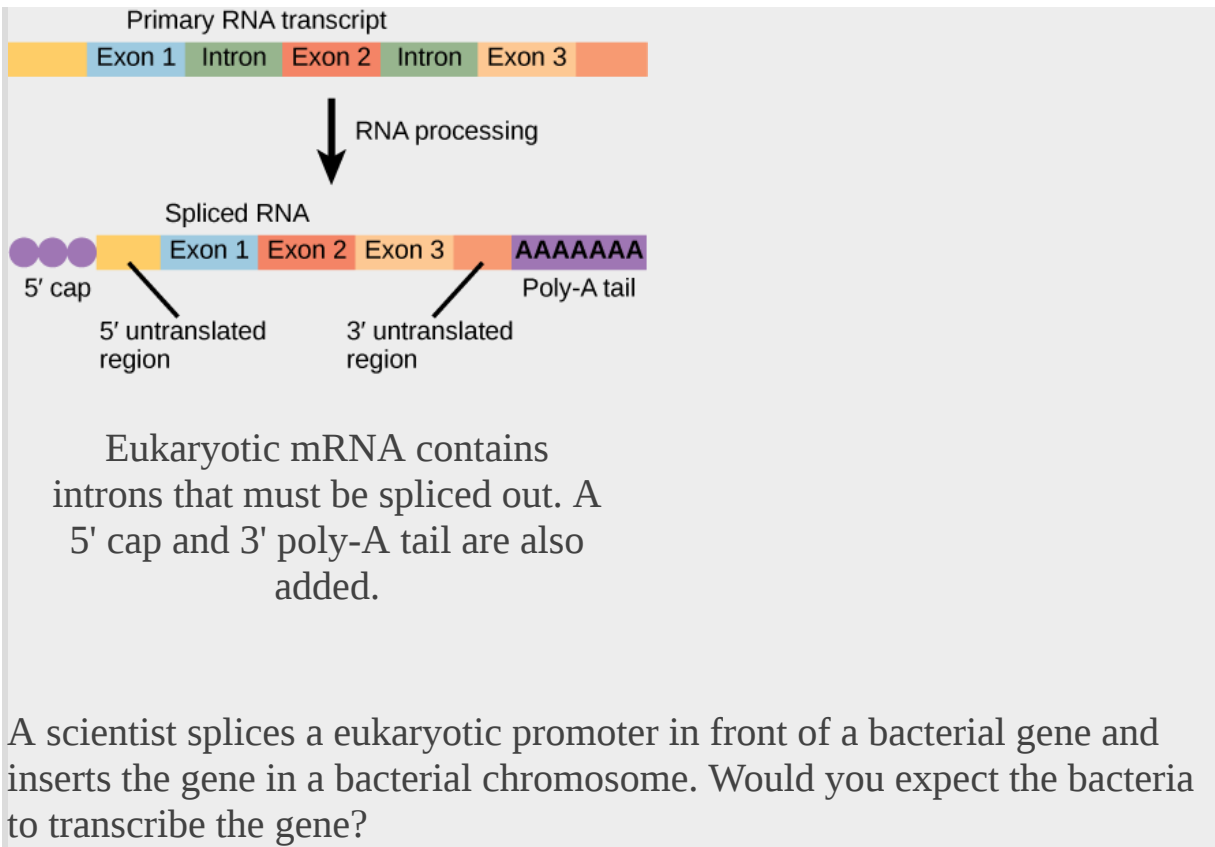
Eukaryotic promoters are much larger and more complex than prokaryotic promoters, but both have a TATA box. For example, in the mouse thymidine kinase gene, the TATA box is located at approximately -30 relative to the initiation (+1) site ([\[link\]](#)). For this gene, the exact TATA box sequence is TATAAAA, as read in the 5' to 3' direction on the nontemplate strand. This sequence is not identical to the *E. coli* TATA box, but it conserves the A–T rich element. The thermostability of A–T bonds is low and this helps the DNA template to locally unwind in preparation for transcription.



A generalized promoter of a gene transcribed by RNA polymerase II is shown.

Transcription factors recognize the promoter. RNA polymerase II then binds and forms the transcription initiation complex.

Note:
Art Connection



The mouse genome includes one gene and two pseudogenes for cytoplasmic thymidine kinase. Pseudogenes are genes that have lost their protein-coding ability or are no longer expressed by the cell. These pseudogenes are copied from mRNA and incorporated into the chromosome. For example, the mouse thymidine kinase promoter also has a conserved **CAAT box** (GGCCAATCT) at approximately -80. This sequence is essential and is involved in binding transcription factors. Further upstream of the TATA box, eukaryotic promoters may also contain one or more **GC-rich boxes** (GGCG) or **octamer boxes** (ATTTGCAT). These elements bind cellular factors that increase the efficiency of transcription initiation and are often identified in more “active” genes that are constantly being expressed by the cell.

Transcription Factors for RNA Polymerase II

The complexity of eukaryotic transcription does not end with the polymerases and promoters. An army of basal transcription factors, enhancers, and silencers also help to regulate the frequency with which pre-mRNA is synthesized from a gene. Enhancers and silencers affect the efficiency of transcription but are not necessary for transcription to proceed. Basal transcription factors are crucial in the formation of a **preinitiation complex** on the DNA template that subsequently recruits RNA polymerase II for transcription initiation.

The names of the basal transcription factors begin with “TFII” (this is the transcription factor for RNA polymerase II) and are specified with the letters A–J. The transcription factors systematically fall into place on the DNA template, with each one further stabilizing the preinitiation complex and contributing to the recruitment of RNA polymerase II.

The processes of bringing RNA polymerases I and III to the DNA template involve slightly less complex collections of transcription factors, but the general theme is the same. Eukaryotic transcription is a tightly regulated process that requires a variety of proteins to interact with each other and with the DNA strand. Although the process of transcription in eukaryotes involves a greater metabolic investment than in prokaryotes, it ensures that the cell transcribes precisely the pre-mRNAs that it needs for protein synthesis.

Note:

Evolution Connection

The Evolution of Promoters

The evolution of genes may be a familiar concept. Mutations can occur in genes during DNA replication, and the result may or may not be beneficial to the cell. By altering an enzyme, structural protein, or some other factor, the process of mutation can transform functions or physical features.

However, eukaryotic promoters and other gene regulatory sequences may evolve as well. For instance, consider a gene that, over many generations, becomes more valuable to the cell. Maybe the gene encodes a structural protein that the cell needs to synthesize in abundance for a certain function. If this is the case, it would be beneficial to the cell for that gene’s promoter

to recruit transcription factors more efficiently and increase gene expression.

Scientists examining the evolution of promoter sequences have reported varying results. In part, this is because it is difficult to infer exactly where a eukaryotic promoter begins and ends. Some promoters occur within genes; others are located very far upstream, or even downstream, of the genes they are regulating. However, when researchers limited their examination to human core promoter sequences that were defined experimentally as sequences that bind the preinitiation complex, they found that promoters evolve even faster than protein-coding genes.

It is still unclear how promoter evolution might correspond to the evolution of humans or other higher organisms. However, the evolution of a promoter to effectively make more or less of a given gene product is an intriguing alternative to the evolution of the genes themselves. [\[footnote\]](#)

H Liang et al., “Fast evolution of core promoters in primate genomes,” *Molecular Biology and Evolution* 25 (2008): 1239–44.

Promoter Structures for RNA Polymerases I and III

In eukaryotes, the conserved promoter elements differ for genes transcribed by RNA polymerases I, II, and III. RNA polymerase I transcribes genes that have two GC-rich promoter sequences in the -45 to +20 region. These sequences alone are sufficient for transcription initiation to occur, but promoters with additional sequences in the region from -180 to -105 upstream of the initiation site will further enhance initiation. Genes that are transcribed by RNA polymerase III have upstream promoters or promoters that occur within the genes themselves.

Eukaryotic Elongation and Termination

Following the formation of the preinitiation complex, the polymerase is released from the other transcription factors, and elongation is allowed to proceed as it does in prokaryotes with the polymerase synthesizing pre-mRNA in the 5' to 3' direction. As discussed previously, RNA polymerase

II transcribes the major share of eukaryotic genes, so this section will focus on how this polymerase accomplishes elongation and termination.

Although the enzymatic process of elongation is essentially the same in eukaryotes and prokaryotes, the DNA template is more complex. When eukaryotic cells are not dividing, their genes exist as a diffuse mass of DNA and proteins called chromatin. The DNA is tightly packaged around charged histone proteins at repeated intervals. These DNA–histone complexes, collectively called nucleosomes, are regularly spaced and include 146 nucleotides of DNA wound around eight histones like thread around a spool.

For polynucleotide synthesis to occur, the transcription machinery needs to move histones out of the way every time it encounters a nucleosome. This is accomplished by a special protein complex called **FACT**, which stands for “facilitates chromatin transcription.” This complex pulls histones away from the DNA template as the polymerase moves along it. Once the pre-mRNA is synthesized, the FACT complex replaces the histones to recreate the nucleosomes.

The termination of transcription is different for the different polymerases. Unlike in prokaryotes, elongation by RNA polymerase II in eukaryotes takes place 1,000–2,000 nucleotides beyond the end of the gene being transcribed. This pre-mRNA tail is subsequently removed by cleavage during mRNA processing. On the other hand, RNA polymerases I and III require termination signals. Genes transcribed by RNA polymerase I contain a specific 18-nucleotide sequence that is recognized by a termination protein. The process of termination in RNA polymerase III involves an mRNA hairpin similar to rho-independent termination of transcription in prokaryotes.

Section Summary

Transcription in eukaryotes involves one of three types of polymerases, depending on the gene being transcribed. RNA polymerase II transcribes all of the protein-coding genes, whereas RNA polymerase I transcribes rRNA genes, and RNA polymerase III transcribes rRNA, tRNA, and small nuclear

RNA genes. The initiation of transcription in eukaryotes involves the binding of several transcription factors to complex promoter sequences that are usually located upstream of the gene being copied. The mRNA is synthesized in the 5' to 3' direction, and the FACT complex moves and reassembles nucleosomes as the polymerase passes by. Whereas RNA polymerases I and III terminate transcription by protein- or RNA hairpin-dependent methods, RNA polymerase II transcribes for 1,000 or more nucleotides beyond the gene template and cleaves the excess during pre-mRNA processing.

Art Connections

Exercise:

Problem:

[\[link\]](#) A scientist splices a eukaryotic promoter in front of a bacterial gene and inserts the gene in a bacterial chromosome. Would you expect the bacteria to transcribe the gene?

Solution:

[\[link\]](#) No. Prokaryotes use different promoters than eukaryotes.

Review Questions

Exercise:

Problem:

Which feature of promoters can be found in both prokaryotes and eukaryotes?

- a. GC box
- b. TATA box
- c. octamer box
- d. -10 and -35 sequences

Solution:

B

Exercise:

Problem:

What transcripts will be most affected by low levels of α -amanitin?

- a. 18S and 28S rRNAs
- b. pre-mRNAs
- c. 5S rRNAs and tRNAs
- d. other small nuclear RNAs

Solution:

B

Glossary

CAAT box

(GGCCAATCT) essential eukaryotic promoter sequence involved in binding transcription factors

FACT

complex that “facilitates chromatin transcription” by disassembling nucleosomes ahead of a transcribing RNA polymerase II and reassembling them after the polymerase passes by

GC-rich box

(GGCG) nonessential eukaryotic promoter sequence that binds cellular factors to increase the efficiency of transcription; may be present several times in a promoter

Octamer box

(ATTTGCAT) nonessential eukaryotic promoter sequence that binds cellular factors to increase the efficiency of transcription; may be present several times in a promoter

preinitiation complex

cluster of transcription factors and other proteins that recruit RNA polymerase II for transcription of a DNA template

small nuclear RNA

molecules synthesized by RNA polymerase III that have a variety of functions, including splicing pre-mRNAs and regulating transcription factors

Bis2A 12.3 RNA Processing in Eukaryotes

By the end of this section, you will be able to:

- Describe the different steps in RNA processing
- Understand the significance of exons, introns, and splicing
- Explain how tRNAs and rRNAs are processed

After transcription, eukaryotic pre-mRNAs must undergo several processing steps before they can be translated. Eukaryotic (and prokaryotic) tRNAs and rRNAs also undergo processing before they can function as components in the protein synthesis machinery.

mRNA Processing

The eukaryotic pre-mRNA undergoes extensive processing before it is ready to be translated. The additional steps involved in eukaryotic mRNA maturation create a molecule with a much longer half-life than a prokaryotic mRNA. Eukaryotic mRNAs last for several hours, whereas the typical *E. coli* mRNA lasts no more than five seconds.

Pre-mRNAs are first coated in RNA-stabilizing proteins; these protect the pre-mRNA from degradation while it is processed and exported out of the nucleus. The three most important steps of pre-mRNA processing are the addition of stabilizing and signaling factors at the 5' and 3' ends of the molecule, and the removal of intervening sequences that do not specify the appropriate amino acids. In rare cases, the mRNA transcript can be “edited” after it is transcribed.

Note:

Evolution Connection

RNA Editing in Trypanosomes

The trypanosomes are a group of protozoa that include the pathogen *Trypanosoma brucei*, which causes sleeping sickness in humans ([link](#)). Trypanosomes, and virtually all other eukaryotes, have organelles called mitochondria that supply the cell with chemical energy. Mitochondria are

organelles that express their own DNA and are believed to be the remnants of a symbiotic relationship between a eukaryote and an engulfed prokaryote. The mitochondrial DNA of trypanosomes exhibit an interesting exception to The Central Dogma: their pre-mRNAs do not have the correct information to specify a functional protein. Usually, this is because the mRNA is missing several U nucleotides. The cell performs an additional RNA processing step called **RNA editing** to remedy this.



Trypanosoma brucei is the causative agent of sleeping sickness in humans. The mRNAs of this pathogen must be modified by the addition of nucleotides before protein synthesis can occur. (credit: modification of work by Torsten Ochsenreiter)

Other genes in the mitochondrial genome encode 40- to 80-nucleotide guide RNAs. One or more of these molecules interacts by complementary base pairing with some of the nucleotides in the pre-mRNA transcript. However, the guide RNA has more A nucleotides than the pre-mRNA has U nucleotides to bind with. In these regions, the guide RNA loops out. The

3' ends of guide RNAs have a long poly-U tail, and these U bases are inserted in regions of the pre-mRNA transcript at which the guide RNAs are looped. This process is entirely mediated by RNA molecules. That is, guide RNAs—rather than proteins—serve as the catalysts in RNA editing. RNA editing is not just a phenomenon of trypanosomes. In the mitochondria of some plants, almost all pre-mRNAs are edited. RNA editing has also been identified in mammals such as rats, rabbits, and even humans. What could be the evolutionary reason for this additional step in pre-mRNA processing? One possibility is that the mitochondria, being remnants of ancient prokaryotes, have an equally ancient RNA-based method for regulating gene expression. In support of this hypothesis, edits made to pre-mRNAs differ depending on cellular conditions. Although speculative, the process of RNA editing may be a holdover from a primordial time when RNA molecules, instead of proteins, were responsible for catalyzing reactions.

5' Capping

While the pre-mRNA is still being synthesized, a **7-methylguanosine cap** is added to the 5' end of the growing transcript by a phosphate linkage. This moiety (functional group) protects the nascent mRNA from degradation. In addition, factors involved in protein synthesis recognize the cap to help initiate translation by ribosomes.

3' Poly-A Tail

Once elongation is complete, the pre-mRNA is cleaved by an endonuclease between an AAUAAA consensus sequence and a GU-rich sequence, leaving the AAUAAA sequence on the pre-mRNA. An enzyme called poly-A polymerase then adds a string of approximately 200 A residues, called the **poly-A tail**. This modification further protects the pre-mRNA from degradation and signals the export of the cellular factors that the transcript needs to the cytoplasm.

Pre-mRNA Splicing

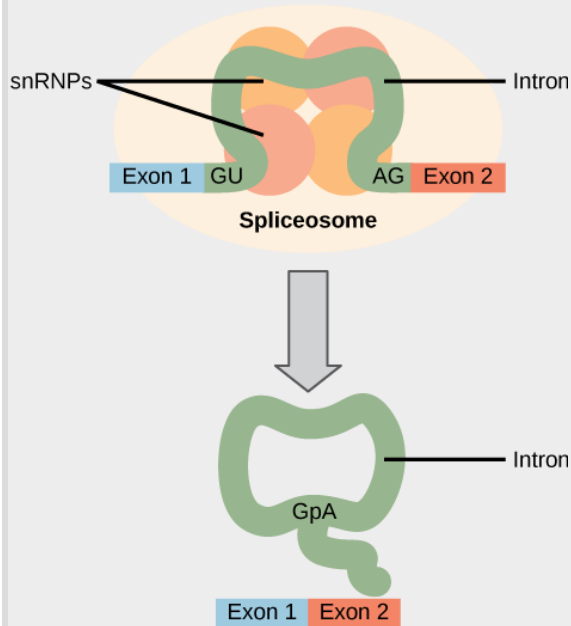
Eukaryotic genes are composed of **exons**, which correspond to protein-coding sequences (*ex-on* signifies that they are *expressed*), and *intervening* sequences called **introns** (*int-ron* denotes their *intervening* role), which may be involved in gene regulation but are removed from the pre-mRNA during processing. Intron sequences in mRNA do not encode functional proteins.

The discovery of introns came as a surprise to researchers in the 1970s who expected that pre-mRNAs would specify protein sequences without further processing, as they had observed in prokaryotes. The genes of higher eukaryotes very often contain one or more introns. These regions may correspond to regulatory sequences; however, the biological significance of having many introns or having very long introns in a gene is unclear. It is possible that introns slow down gene expression because it takes longer to transcribe pre-mRNAs with lots of introns. Alternatively, introns may be nonfunctional sequence remnants left over from the fusion of ancient genes throughout evolution. This is supported by the fact that separate exons often encode separate protein subunits or domains. For the most part, the sequences of introns can be mutated without ultimately affecting the protein product.

All of a pre-mRNA's introns must be completely and precisely removed before protein synthesis. If the process errs by even a single nucleotide, the reading frame of the rejoined exons would shift, and the resulting protein would be dysfunctional. The process of removing introns and reconnecting exons is called **splicing** ([\[link\]](#)). Introns are removed and degraded while the pre-mRNA is still in the nucleus. Splicing occurs by a sequence-specific mechanism that ensures introns will be removed and exons rejoined with the accuracy and precision of a single nucleotide. The splicing of pre-mRNAs is conducted by complexes of proteins and RNA molecules called spliceosomes.

Note:

Art Connection



Pre-mRNA splicing involves the precise removal of introns from the primary RNA transcript. The splicing process is catalyzed by protein complexes called spliceosomes that are composed of proteins and RNA molecules called snRNAs. Spliceosomes recognize sequences at the 5' and 3' end of the intron.

Errors in splicing are implicated in cancers and other human diseases. What kinds of mutations might lead to splicing errors? Think of different possible outcomes if splicing errors occur.

Note that more than 70 individual introns can be present, and each has to undergo the process of splicing—in addition to 5' capping and the addition

of a poly-A tail—just to generate a single, translatable mRNA molecule.

Note:

Link to Learning



See how introns are removed during RNA splicing [at this website](#).

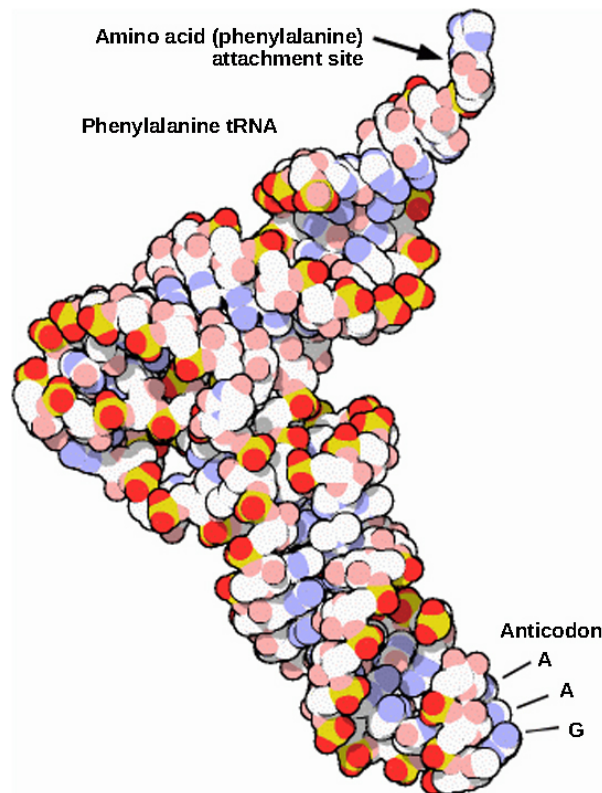
Processing of tRNAs and rRNAs

The tRNAs and rRNAs are structural molecules that have roles in protein synthesis; however, these RNAs are not themselves translated. Pre-rRNAs are transcribed, processed, and assembled into ribosomes in the nucleolus. Pre-tRNAs are transcribed and processed in the nucleus and then released into the cytoplasm where they are linked to free amino acids for protein synthesis.

Most of the tRNAs and rRNAs in eukaryotes and prokaryotes are first transcribed as a long precursor molecule that spans multiple rRNAs or tRNAs. Enzymes then cleave the precursors into subunits corresponding to each structural RNA. Some of the bases of pre-rRNAs are methylated; that is, a -CH_3 moiety (methyl functional group) is added for stability. Pre-tRNA molecules also undergo methylation. As with pre-mRNAs, subunit excision occurs in eukaryotic pre-RNAs destined to become tRNAs or rRNAs.

Mature rRNAs make up approximately 50 percent of each ribosome. Some of a ribosome's RNA molecules are purely structural, whereas others have catalytic or binding activities. Mature tRNAs take on a three-dimensional

structure through intramolecular hydrogen bonding to position the amino acid binding site at one end and the **anticodon** at the other end ([\[link\]](#)). The anticodon is a three-nucleotide sequence in a tRNA that interacts with an mRNA codon through complementary base pairing.



This is a space-filling model of a tRNA molecule that adds the amino acid phenylalanine to a growing polypeptide chain. The anticodon AAG binds the Codon UUC on the mRNA. The amino acid phenylalanine is attached to the other end of the tRNA.

Section Summary

Eukaryotic pre-mRNAs are modified with a 5' methylguanosine cap and a poly-A tail. These structures protect the mature mRNA from degradation and help export it from the nucleus. Pre-mRNAs also undergo splicing, in which introns are removed and exons are reconnected with single-nucleotide accuracy. Only finished mRNAs that have undergone 5' capping, 3' polyadenylation, and intron splicing are exported from the nucleus to the cytoplasm. Pre-rRNAs and pre-tRNAs may be processed by intramolecular cleavage, splicing, methylation, and chemical conversion of nucleotides. Rarely, RNA editing is also performed to insert missing bases after an mRNA has been synthesized.

Art Connections

Exercise:

Problem:

[\[link\]](#) Errors in splicing are implicated in cancers and other human diseases. What kinds of mutations might lead to splicing errors? Think of different possible outcomes if splicing errors occur.

Solution:

[\[link\]](#) Mutations in the spliceosome recognition sequence at each end of the intron, or in the proteins and RNAs that make up the spliceosome, may impair splicing. Mutations may also add new spliceosome recognition sites. Splicing errors could lead to introns being retained in spliced RNA, exons being excised, or changes in the location of the splice site.

Review Questions

Exercise:

Problem:

Which pre-mRNA processing step is important for initiating translation?

- a. poly-A tail
- b. RNA editing
- c. splicing
- d. 7-methylguanosine cap

Solution:

D

Exercise:**Problem:**

What processing step enhances the stability of pre-tRNAs and pre-rRNAs?

- a. methylation
- b. nucleotide modification
- c. cleavage
- d. splicing

Solution:

A

Glossary

7-methylguanosine cap

modification added to the 5' end of pre-mRNAs to protect mRNA from degradation and assist translation

anticodon

three-nucleotide sequence in a tRNA molecule that corresponds to an mRNA codon

exon

sequence present in protein-coding mRNA after completion of pre-mRNA splicing

intron

non-protein-coding intervening sequences that are spliced from mRNA during processing

poly-A tail

modification added to the 3' end of pre-mRNAs to protect mRNA from degradation and assist mRNA export from the nucleus

RNA editing

direct alteration of one or more nucleotides in an mRNA that has already been synthesized

splicing

process of removing introns and reconnecting exons in a pre-mRNA

Bis2A 13.0 Translation

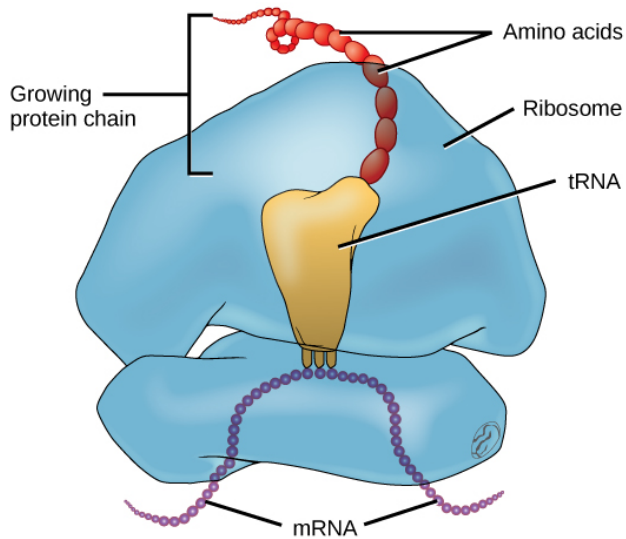
By the end of this section, you will be able to:

- Describe the different steps in protein synthesis
- Discuss the role of ribosomes in protein synthesis
- Describe the genetic code and how the nucleotide sequence determines the amino acid and the protein sequence

The synthesis of proteins is one of a cell's most energy-consuming metabolic processes. In turn, proteins account for more mass than any other component of living organisms (with the exception of water), and proteins perform a wide variety of the functions of a cell. The process of translation, or protein synthesis, involves decoding an mRNA message into a polypeptide product. Amino acids are covalently strung together in lengths ranging from approximately 50 amino acids to more than 1,000.

The Protein Synthesis Machinery

In addition to the mRNA template, many other molecules contribute to the process of translation. The composition of each component may vary across species; for instance, ribosomes may consist of different numbers of ribosomal RNAs (**rRNA**) and polypeptides depending on the organism. However, the general structures and functions of the protein synthesis machinery are comparable from bacteria to human cells. Translation requires the input of an mRNA template, ribosomes, tRNAs, and various enzymatic factors ([\[link\]](#)).



The protein synthesis machinery includes the large and small subunits of the ribosome, mRNA, and tRNA. (credit: modification of work by NIGMS, NIH)

In *E. coli*, there are 200,000 ribosomes present in every cell at any given time. A ribosome is a complex macromolecule composed of structural and catalytic rRNAs, and many distinct polypeptides. In eukaryotes, the nucleolus is completely specialized for the synthesis and assembly of rRNAs.

Ribosomes are located in the cytoplasm in prokaryotes and in the cytoplasm and endoplasmic reticulum of eukaryotes. Ribosomes are made up of a large and a small subunit that come together for translation. The small subunit is responsible for binding the mRNA template, whereas the large subunit sequentially binds **tRNAs**, a type of RNA molecule that brings amino acids to the growing chain of the polypeptide. Each mRNA molecule is simultaneously translated by many ribosomes, all synthesizing protein in the same direction.

Depending on the species, 40 to 60 types of tRNA exist in the cytoplasm. Serving as adaptors, specific tRNAs bind to sequences on the mRNA

template and add the corresponding amino acid to the polypeptide chain. Therefore, tRNAs are the molecules that actually “translate” the language of RNA into the language of proteins. For each tRNA to function, it must have its specific amino acid bonded to it. In the process of tRNA “charging,” each tRNA molecule is bonded to its correct amino acid.

The Genetic Code

To summarize what we know to this point, the cellular process of transcription generates messenger RNA (mRNA), a mobile molecular copy of one or more genes with an alphabet of A, C, G, and uracil (U). Translation of the mRNA template converts nucleotide-based genetic information into a protein product. Protein sequences consist of 20 commonly occurring amino acids; therefore, it can be said that the protein alphabet consists of 20 letters. Each amino acid is defined by a three-nucleotide sequence called the triplet **codon**. The relationship between a nucleotide codon and its corresponding amino acid is called the **genetic code**.

Given the different numbers of “letters” in the mRNA and protein “alphabets,” combinations of nucleotides corresponded to single amino acids. Using a three-nucleotide code means that there are a total of 64 ($4 \times 4 \times 4$) possible combinations; therefore, a given amino acid is encoded by more than one nucleotide triplet ([\[link\]](#)).

		Second letter					
		U	C	A	G		
First letter	U	UUU } Phe UUC } UUA } Leu UUG }	UCU } UCC } Ser UCA } UCG }	UAU } Tyr UAC } UAA Stop UAG Stop	UGU } Cys UGC } UGA Stop UGG Trp	U C A G	Third letter
	C	CUU } CUC } Leu CUA } CUG }	CCU } CCC } Pro CCA } CCG }	CAU } His CAC } CAA } Gln CAG }	CGU } CGC } Arg CGA } CGG }	U C A G	
	A	AUU } AUC } Ile AUA } AUG Met	ACU } ACC } Thr ACA } ACG }	AAU } Asn AAC } AAA } Lys AAG }	AGU } Ser AGC } AGA } Arg AGG }	U C A G	
	G	GUU } GUC } Val GUA } GUG }	GCU } GCC } Ala GCA } GCG }	GAU } Asp GAC } GAA } Glu GAG }	GGU } GGC } Gly GGA } GGG }	U C A G	

This figure shows the genetic code for translating each nucleotide triplet, or codon, in mRNA into an amino acid or a termination signal in a nascent protein. (credit: modification of work by NIH)

Three of the 64 codons terminate protein synthesis and release the polypeptide from the translation machinery. These triplets are called **stop codons**. Another codon, AUG, also has a special function. In addition to specifying the amino acid methionine, it also serves as the **start codon** to initiate translation. The reading frame for translation is set by the AUG start codon near the 5' end of the mRNA. The genetic code is universal. With a few exceptions, virtually all species use the same genetic code for protein synthesis, which is powerful evidence that all life on Earth shares a common origin.

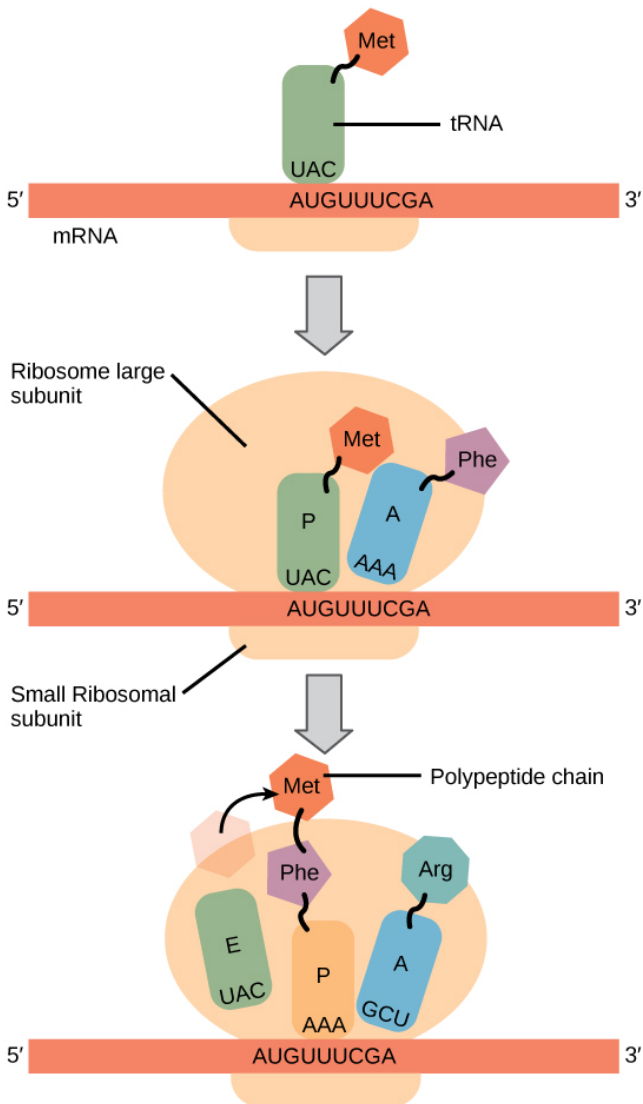
The Mechanism of Protein Synthesis

Just as with mRNA synthesis, protein synthesis can be divided into three phases: initiation, elongation, and termination. The process of translation is

similar in prokaryotes and eukaryotes. Here we will explore how translation occurs in *E. coli*, a representative prokaryote, and specify any differences between prokaryotic and eukaryotic translation.

Protein synthesis begins with the formation of an initiation complex. In *E. coli*, this complex involves the small ribosome subunit, the mRNA template, three initiation factors, and a special initiator tRNA. The initiator tRNA interacts with the AUG start codon, and links to a special form of the amino acid methionine that is typically removed from the polypeptide after translation is complete.

In prokaryotes and eukaryotes, the basics of polypeptide elongation are the same, so we will review elongation from the perspective of *E. coli*. The large ribosomal subunit of *E. coli* consists of three compartments: the A site binds incoming charged tRNAs (tRNAs with their attached specific amino acids). The P site binds charged tRNAs carrying amino acids that have formed bonds with the growing polypeptide chain but have not yet dissociated from their corresponding tRNA. The E site releases dissociated tRNAs so they can be recharged with free amino acids. The ribosome shifts one codon at a time, catalyzing each process that occurs in the three sites. With each step, a charged tRNA enters the complex, the polypeptide becomes one amino acid longer, and an uncharged tRNA departs. The energy for each bond between amino acids is derived from GTP, a molecule similar to ATP ([\[link\]](#)). Amazingly, the *E. coli* translation apparatus takes only 0.05 seconds to add each amino acid, meaning that a 200-amino acid polypeptide could be translated in just 10 seconds.



Translation begins when a tRNA anticodon recognizes a codon on the mRNA. The large ribosomal subunit joins the small subunit, and a second tRNA is recruited. As the mRNA moves relative to the ribosome, the polypeptide chain is formed. Entry of a release factor into the A site terminates translation and the components dissociate.

Termination of translation occurs when a stop codon (UAA, UAG, or UGA) is encountered. When the ribosome encounters the stop codon, the growing polypeptide is released and the ribosome subunits dissociate and leave the mRNA. After many ribosomes have completed translation, the mRNA is degraded so the nucleotides can be reused in another transcription reaction.

Note:**Concept in Action**

Transcribe a gene and translate it to protein using complementary pairing and the genetic code at [this site](#).

Section Summary

The central dogma describes the flow of genetic information in the cell from genes to mRNA to proteins. Genes are used to make mRNA by the process of transcription; mRNA is used to synthesize proteins by the process of translation. The genetic code is the correspondence between the three-nucleotide mRNA codon and an amino acid. The genetic code is “translated” by the tRNA molecules, which associate a specific codon with a specific amino acid. The genetic code is degenerate because 64 triplet codons in mRNA specify only 20 amino acids and three stop codons. This means that more than one codon corresponds to an amino acid. Almost every species on the planet uses the same genetic code.

The players in translation include the mRNA template, ribosomes, tRNAs, and various enzymatic factors. The small ribosomal subunit binds to the mRNA template. Translation begins at the initiating AUG on the mRNA. The formation of bonds occurs between sequential amino acids specified by the mRNA template according to the genetic code. The ribosome accepts charged tRNAs, and as it steps along the mRNA, it catalyzes bonding between the new amino acid and the end of the growing polypeptide. The entire mRNA is translated in three-nucleotide “steps” of the ribosome. When a stop codon is encountered, a release factor binds and dissociates the components and frees the new protein.

Multiple Choice

Exercise:

Problem:

The RNA components of ribosomes are synthesized in the _____.

- a. cytoplasm
- b. nucleus
- c. nucleolus
- d. endoplasmic reticulum

Solution:

C

Exercise:

Problem:

How long would the peptide be that is translated from this MRNA sequence: 5'-AUGGGCUACCGA-3'?

- a. 0
- b. 2
- c. 3

d. 4

Solution:

D

Free Response

Exercise:

Problem:

Transcribe and translate the following DNA sequence (nontemplate strand): 5'-ATGGCCGGTTATTAAGCA-3'

Solution:

The mRNA would be: 5'-AUGGCCGGUUAUUAAGCA-3'. The protein would be: MAGY. Even though there are six codons, the fifth codon corresponds to a stop, so the sixth codon would not be translated.

Glossary

codon

three consecutive nucleotides in mRNA that specify the addition of a specific amino acid or the release of a polypeptide chain during translation

genetic code

the amino acids that correspond to three-nucleotide codons of mRNA

rRNA

ribosomal RNA; molecules of RNA that combine to form part of the ribosome

stop codon

one of the three mRNA codons that specifies termination of translation

start codon

the AUG (or, rarely GUG) on an mRNA from which translation begins; always specifies methionine

tRNA

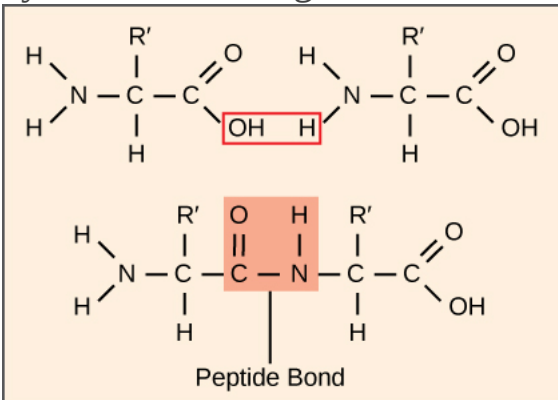
transfer RNA; an RNA molecule that contains a specific three-nucleotide anticodon sequence to pair with the mRNA codon and also binds to a specific amino acid

Bis2A 13.1 Ribosomes and Protein Synthesis

By the end of this section, you will be able to:

- Describe the different steps in protein synthesis
- Discuss the role of ribosomes in protein synthesis

The synthesis of proteins consumes more of a cell's energy than any other metabolic process. In turn, proteins account for more mass than any other component of living organisms (with the exception of water), and proteins perform virtually every function of a cell. The process of translation, or protein synthesis, involves the decoding of an mRNA message into a polypeptide product. Amino acids are covalently strung together by interlinking peptide bonds in lengths ranging from approximately 50 amino acid residues to more than 1,000. Each individual amino acid has an amino group (NH_2) and a carboxyl (COOH) group. Polypeptides are formed when the amino group of one amino acid forms an amide (i.e., peptide) bond with the carboxyl group of another amino acid ([\[link\]](#)). This reaction is catalyzed by ribosomes and generates one water molecule.



A peptide bond links the carboxyl end of one amino acid with the amino end of another, expelling one water molecule. For simplicity in this image, only the functional groups involved in the peptide bond are shown. The R and R' designations

refer to the rest of each amino acid structure.

The Protein Synthesis Machinery

In addition to the mRNA template, many molecules and macromolecules contribute to the process of translation. The composition of each component may vary across species; for instance, ribosomes may consist of different numbers of rRNAs and polypeptides depending on the organism. However, the general structures and functions of the protein synthesis machinery are comparable from bacteria to human cells. Translation requires the input of an mRNA template, ribosomes, tRNAs, and various enzymatic factors.

Note:

Link to Learning



Click through the steps of this [PBS interactive](#) to see protein synthesis in action.

Ribosomes

Even before an mRNA is translated, a cell must invest energy to build each of its ribosomes. In *E. coli*, there are between 10,000 and 70,000 ribosomes present in each cell at any given time. A ribosome is a complex macromolecule composed of structural and catalytic rRNAs, and many distinct polypeptides. In eukaryotes, the nucleolus is completely specialized for the synthesis and assembly of rRNAs.

Ribosomes exist in the cytoplasm in prokaryotes and in the cytoplasm and rough endoplasmic reticulum in eukaryotes. Mitochondria and chloroplasts also have their own ribosomes in the matrix and stroma, which look more similar to prokaryotic ribosomes (and have similar drug sensitivities) than the ribosomes just outside their outer membranes in the cytoplasm.

Ribosomes dissociate into large and small subunits when they are not synthesizing proteins and reassociate during the initiation of translation. In *E. coli*, the small subunit is described as 30S, and the large subunit is 50S, for a total of 70S (recall that Svedberg units are not additive). Mammalian ribosomes have a small 40S subunit and a large 60S subunit, for a total of 80S. The small subunit is responsible for binding the mRNA template, whereas the large subunit sequentially binds tRNAs. Each mRNA molecule is simultaneously translated by many ribosomes, all synthesizing protein in the same direction: reading the mRNA from 5' to 3' and synthesizing the polypeptide from the N terminus to the C terminus. The complete mRNA/poly-ribosome structure is called a **polysome**.

tRNAs

The tRNAs are structural RNA molecules that were transcribed from genes by RNA polymerase III. Depending on the species, 40 to 60 types of tRNAs exist in the cytoplasm. Serving as adaptors, specific tRNAs bind to sequences on the mRNA template and add the corresponding amino acid to the polypeptide chain. Therefore, tRNAs are the molecules that actually “translate” the language of RNA into the language of proteins.

Of the 64 possible mRNA codons—or triplet combinations of A, U, G, and C—three specify the termination of protein synthesis and 61 specify the addition of amino acids to the polypeptide chain. Of these 61, one codon (AUG) also encodes the initiation of translation. Each tRNA anticodon can base pair with one of the mRNA codons and add an amino acid or terminate translation, according to the genetic code. For instance, if the sequence CUA occurred on an mRNA template in the proper reading frame, it would bind a tRNA expressing the complementary sequence, GAU, which would be linked to the amino acid leucine.

As the adaptor molecules of translation, it is surprising that tRNAs can fit so much specificity into such a small package. Consider that tRNAs need to interact with three factors: 1) they must be recognized by the correct aminoacyl synthetase (see below); 2) they must be recognized by ribosomes; and 3) they must bind to the correct sequence in mRNA.

Aminoacyl tRNA Synthetases

The process of pre-tRNA synthesis by RNA polymerase III only creates the RNA portion of the adaptor molecule. The corresponding amino acid must be added later, once the tRNA is processed and exported to the cytoplasm. Through the process of tRNA “charging,” each tRNA molecule is linked to its correct amino acid by a group of enzymes called **aminoacyl tRNA synthetases**. At least one type of aminoacyl tRNA synthetase exists for each of the 20 amino acids; the exact number of aminoacyl tRNA synthetases varies by species. These enzymes first bind and hydrolyze ATP to catalyze a high-energy bond between an amino acid and adenosine monophosphate (AMP); a pyrophosphate molecule is expelled in this reaction. The activated amino acid is then transferred to the tRNA, and AMP is released.

The Mechanism of Protein Synthesis

As with mRNA synthesis, protein synthesis can be divided into three phases: initiation, elongation, and termination. The process of translation is similar in prokaryotes and eukaryotes. Here we’ll explore how translation occurs in *E. coli*, a representative prokaryote, and specify any differences between prokaryotic and eukaryotic translation.

Initiation of Translation

Protein synthesis begins with the formation of an initiation complex. In *E. coli*, this complex involves the small 30S ribosome, the mRNA template, three initiation factors (IFs; IF-1, IF-2, and IF-3), and a special **initiator**

tRNA, called $\text{tRNA}_f^{\text{Met}}$. The initiator tRNA interacts with the **start codon** AUG (or rarely, GUG), links to a formylated methionine called fMet, and can also bind IF-2. Formylated methionine is inserted by $\text{fMet} - \text{tRNA}_f^{\text{Met}}$ at the beginning of every polypeptide chain synthesized by *E. coli*, but it is usually clipped off after translation is complete. When an in-frame AUG is encountered during translation elongation, a non-formylated methionine is inserted by a regular $\text{Met-tRNA}^{\text{Met}}$.

In *E. coli* mRNA, a sequence upstream of the first AUG codon, called the **Shine-Dalgarno sequence** (AGGAGG), interacts with the rRNA molecules that compose the ribosome. This interaction anchors the 30S ribosomal subunit at the correct location on the mRNA template. Guanosine triphosphate (GTP), which is a purine nucleotide triphosphate, acts as an energy source during translation—both at the start of elongation and during the ribosome's translocation.

In eukaryotes, a similar initiation complex forms, comprising mRNA, the 40S small ribosomal subunit, IFs, and nucleoside triphosphates (GTP and ATP). The charged initiator tRNA, called Met-tRNA_i , does not bind fMet in eukaryotes, but is distinct from other Met-tRNAs in that it can bind IFs.

Instead of depositing at the Shine-Dalgarno sequence, the eukaryotic initiation complex recognizes the 7-methylguanosine cap at the 5' end of the mRNA. A cap-binding protein (CBP) and several other IFs assist the movement of the ribosome to the 5' cap. Once at the cap, the initiation complex tracks along the mRNA in the 5' to 3' direction, searching for the AUG start codon. Many eukaryotic mRNAs are translated from the first AUG, but this is not always the case. According to **Kozak's rules**, the nucleotides around the AUG indicate whether it is the correct start codon. Kozak's rules state that the following consensus sequence must appear around the AUG of vertebrate genes: 5'-gccRccAUGG-3'. The R (for purine) indicates a site that can be either A or G, but cannot be C or U. Essentially, the closer the sequence is to this consensus, the higher the efficiency of translation.

Once the appropriate AUG is identified, the other proteins and CBP dissociate, and the 60S subunit binds to the complex of Met-tRNA_i , mRNA,

and the 40S subunit. This step completes the initiation of translation in eukaryotes.

Translation, Elongation, and Termination

In prokaryotes and eukaryotes, the basics of elongation are the same, so we will review elongation from the perspective of *E. coli*. The 50S ribosomal subunit of *E. coli* consists of three compartments: the A (aminoacyl) site binds incoming charged aminoacyl tRNAs. The P (peptidyl) site binds charged tRNAs carrying amino acids that have formed peptide bonds with the growing polypeptide chain but have not yet dissociated from their corresponding tRNA. The E (exit) site releases dissociated tRNAs so that they can be recharged with free amino acids. There is one exception to this assembly line of tRNAs: in *E. coli*, fMet — tRNA_f^{Met} is capable of entering the P site directly without first entering the A site. Similarly, the eukaryotic Met-tRNA_i, with help from other proteins of the initiation complex, binds directly to the P site. In both cases, this creates an initiation complex with a free A site ready to accept the tRNA corresponding to the first codon after the AUG.

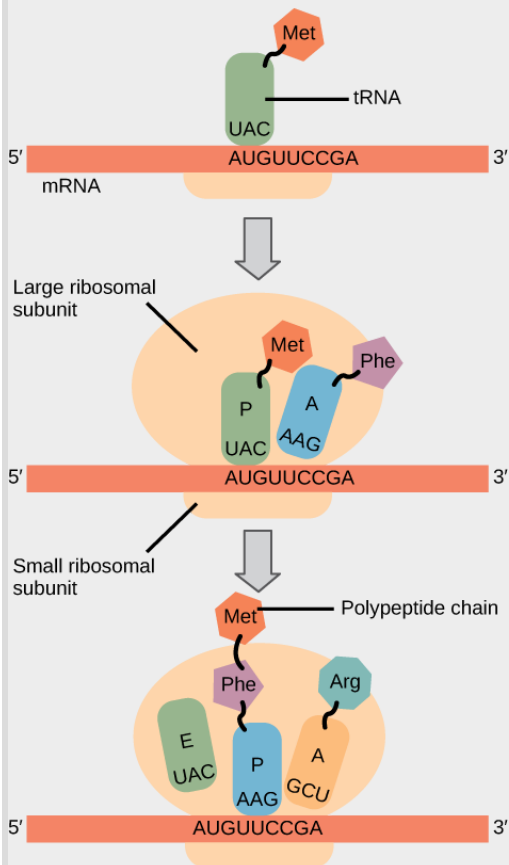
During translation elongation, the mRNA template provides specificity. As the ribosome moves along the mRNA, each mRNA codon comes into register, and specific binding with the corresponding charged tRNA anticodon is ensured. If mRNA were not present in the elongation complex, the ribosome would bind tRNAs nonspecifically.

Elongation proceeds with charged tRNAs entering the A site and then shifting to the P site followed by the E site with each single-codon “step” of the ribosome. Ribosomal steps are induced by conformational changes that advance the ribosome by three bases in the 3' direction. The energy for each step of the ribosome is donated by an elongation factor that hydrolyzes GTP. Peptide bonds form between the amino group of the amino acid attached to the A-site tRNA and the carboxyl group of the amino acid attached to the P-site tRNA. The formation of each peptide bond is catalyzed by **peptidyl transferase**, an RNA-based enzyme that is integrated into the 50S ribosomal subunit. The energy for each peptide bond formation

is derived from GTP hydrolysis, which is catalyzed by a separate elongation factor. The amino acid bound to the P-site tRNA is also linked to the growing polypeptide chain. As the ribosome steps across the mRNA, the former P-site tRNA enters the E site, detaches from the amino acid, and is expelled ([link](#)). Amazingly, the *E. coli* translation apparatus takes only 0.05 seconds to add each amino acid, meaning that a 200-amino acid protein can be translated in just 10 seconds.

Note:

Art Connection



Translation begins when an initiator tRNA anticodon recognizes a codon on mRNA. The large ribosomal subunit

joins the small subunit,
and a second tRNA is
recruited. As the mRNA
moves relative to the
ribosome, the polypeptide
chain is formed. Entry of
a release factor into the A
site terminates translation
and the components
dissociate.

Many antibiotics inhibit bacterial protein synthesis. For example, tetracycline blocks the A site on the bacterial ribosome, and chloramphenicol blocks peptidyl transfer. What specific effect would you expect each of these antibiotics to have on protein synthesis?

Tetracycline would directly affect:

- a. tRNA binding to the ribosome
- b. ribosome assembly
- c. growth of the protein chain

Chloramphenicol would directly affect

- a. tRNA binding to the ribosome
- b. ribosome assembly
- c. growth of the protein chain

Termination of translation occurs when a nonsense codon (UAA, UAG, or UGA) is encountered. Upon aligning with the A site, these nonsense codons are recognized by release factors in prokaryotes and eukaryotes that instruct peptidyl transferase to add a water molecule to the carboxyl end of the P-site amino acid. This reaction forces the P-site amino acid to detach from its tRNA, and the newly made protein is released. The small and large ribosomal subunits dissociate from the mRNA and from each other; they

are recruited almost immediately into another translation initiation complex. After many ribosomes have completed translation, the mRNA is degraded so the nucleotides can be reused in another transcription reaction.

Protein Folding, Modification, and Targeting

During and after translation, individual amino acids may be chemically modified, signal sequences may be appended, and the new protein “folds” into a distinct three-dimensional structure as a result of intramolecular interactions. A **signal sequence** is a short tail of amino acids that directs a protein to a specific cellular compartment. These sequences at the amino end or the carboxyl end of the protein can be thought of as the protein’s “train ticket” to its ultimate destination. Other cellular factors recognize each signal sequence and help transport the protein from the cytoplasm to its correct compartment. For instance, a specific sequence at the amino terminus will direct a protein to the mitochondria or chloroplasts (in plants). Once the protein reaches its cellular destination, the signal sequence is usually clipped off.

Many proteins fold spontaneously, but some proteins require helper molecules, called chaperones, to prevent them from aggregating during the complicated process of folding. Even if a protein is properly specified by its corresponding mRNA, it could take on a completely dysfunctional shape if abnormal temperature or pH conditions prevent it from folding correctly.

Section Summary

The players in translation include the mRNA template, ribosomes, tRNAs, and various enzymatic factors. The small ribosomal subunit forms on the mRNA template either at the Shine-Dalgarno sequence (prokaryotes) or the 5' cap (eukaryotes). Translation begins at the initiating AUG on the mRNA, specifying methionine. The formation of peptide bonds occurs between sequential amino acids specified by the mRNA template according to the genetic code. Charged tRNAs enter the ribosomal A site, and their amino acid bonds with the amino acid at the P site. The entire mRNA is translated in three-nucleotide “steps” of the ribosome. When a nonsense codon is encountered, a release factor binds and dissociates the components and

frees the new protein. Folding of the protein occurs during and after translation.

Art Connections

Exercise:

Problem:

[\[link\]](#) Many antibiotics inhibit bacterial protein synthesis. For example, tetracycline blocks the A site on the bacterial ribosome, and chloramphenicol blocks peptidyl transfer. What specific effect would you expect each of these antibiotics to have on protein synthesis?

Tetracycline would directly affect:

- a. tRNA binding to the ribosome
- b. ribosome assembly
- c. growth of the protein chain

Chloramphenicol would directly affect

- a. tRNA binding to the ribosome
- b. ribosome assembly
- c. growth of the protein chain

Solution:

[\[link\]](#) Tetracycline: a; Chloramphenicol: c.

Review Questions

Exercise:

Problem:

The RNA components of ribosomes are synthesized in the _____.

- a. cytoplasm
 - b. nucleus
 - c. nucleolus
 - d. endoplasmic reticulum
-

Solution:

C

Exercise:

Problem:

In any given species, there are at least how many types of aminoacyl tRNA synthetases?

- a. 20
 - b. 40
 - c. 100
 - d. 200
-

Solution:

A

Free Response

Exercise:

Problem:

Transcribe and translate the following DNA sequence (nontemplate strand): 5'-ATGGCCGGTTATTAAGCA-3'

Solution:

The mRNA would be: 5'-AUGGCCGGUUAUUAAGCA-3'. The protein would be: MAGY. Even though there are six codons, the fifth codon corresponds to a stop, so the sixth codon would not be translated.

Exercise:

Problem:

Explain how single nucleotide changes can have vastly different effects on protein function.

Solution:

Nucleotide changes in the third position of codons may not change the amino acid and would have no effect on the protein. Other nucleotide changes that change important amino acids or create or delete start or stop codons would have severe effects on the amino acid sequence of the protein.

Glossary

aminoacyl tRNA synthetase

enzyme that “charges” tRNA molecules by catalyzing a bond between the tRNA and a corresponding amino acid

initiator tRNA

in prokaryotes, called *fMet*; in eukaryotes, called tRNA_i; a tRNA that interacts with a start codon, binds directly to the ribosome P site, and links to a special methionine to begin a polypeptide chain

Kozak’s rules

determines the correct initiation AUG in a eukaryotic mRNA; the following consensus sequence must appear around the AUG: 5'-GCC(**purine**)CCA**AUG**G-3'; the bolded bases are most important

peptidyl transferase

RNA-based enzyme that is integrated into the 50S ribosomal subunit and catalyzes the formation of peptide bonds

polysome

mRNA molecule simultaneously being translated by many ribosomes all going in the same direction

Shine-Dalgarno sequence

(AGGAGG); initiates prokaryotic translation by interacting with rRNA molecules comprising the 30S ribosome

signal sequence

short tail of amino acids that directs a protein to a specific cellular compartment

start codon

AUG (or rarely, GUG) on an mRNA from which translation begins; always specifies methionine

Bis2A 13.2 Central Dogma Review:

By the end of this section, you will be able to:

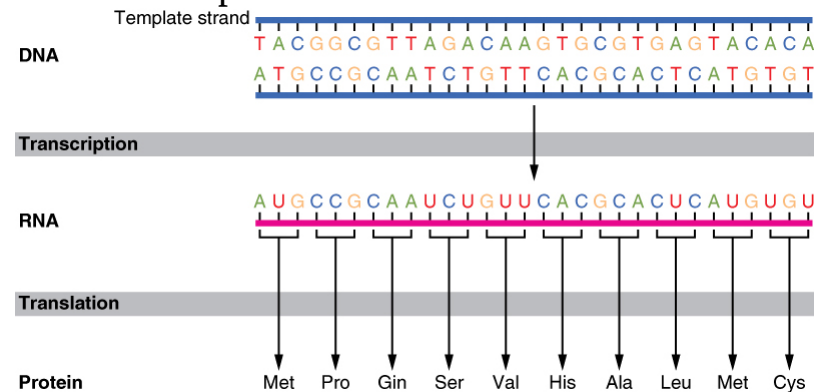
- Explain how the genetic code stored within DNA determines the protein that will form
- Describe the process of transcription
- Describe the process of translation
- Discuss the function of ribosomes

It was mentioned earlier that DNA provides a “blueprint” for the cell structure and physiology. This refers to the fact that DNA contains the information necessary for the cell to build one very important type of molecule: the protein. Most structural components of the cell are made up, at least in part, by proteins and virtually all the functions that a cell carries out are completed with the help of proteins. One of the most important classes of proteins is enzymes, which help speed up necessary biochemical reactions that take place inside the cell. Some of these critical biochemical reactions include building larger molecules from smaller components (such as occurs during DNA replication or synthesis of microtubules) and breaking down larger molecules into smaller components (such as when harvesting chemical energy from nutrient molecules). Whatever the cellular process may be, it is almost sure to involve proteins. Just as the cell’s genome describes its full complement of DNA, a cell’s **proteome** is its full complement of proteins. Protein synthesis begins with genes. A **gene** is a functional segment of DNA that provides the genetic information necessary to build a protein. Each particular gene provides the code necessary to construct a particular protein. **Gene expression**, which transforms the information coded in a gene to a final gene product, ultimately dictates the structure and function of a cell by determining which proteins are made.

The interpretation of genes works in the following way. Recall that proteins are polymers, or chains, of many amino acid building blocks. The sequence of bases in a gene (that is, its sequence of A, T, C, G nucleotides) translates to an amino acid sequence. A **triplet** is a section of three DNA bases in a row that codes for a specific amino acid. Similar to the way in which the three-letter code *d-o-g* signals the image of a dog, the three-letter DNA base code signals the use of a particular amino acid. For example, the DNA

triplet CAC (cytosine, adenine, and cytosine) specifies the amino acid valine. Therefore, a gene, which is composed of multiple triplets in a unique sequence, provides the code to build an entire protein, with multiple amino acids in the proper sequence ([\[link\]](#)). The mechanism by which cells turn the DNA code into a protein product is a two-step process, with an RNA molecule as the intermediate.

The Transcription/Translation Process



DNA holds all of the genetic information necessary to build a cell's proteins. The nucleotide sequence of a gene is ultimately translated into an amino acid sequence of the gene's corresponding protein.

From DNA to RNA: Transcription

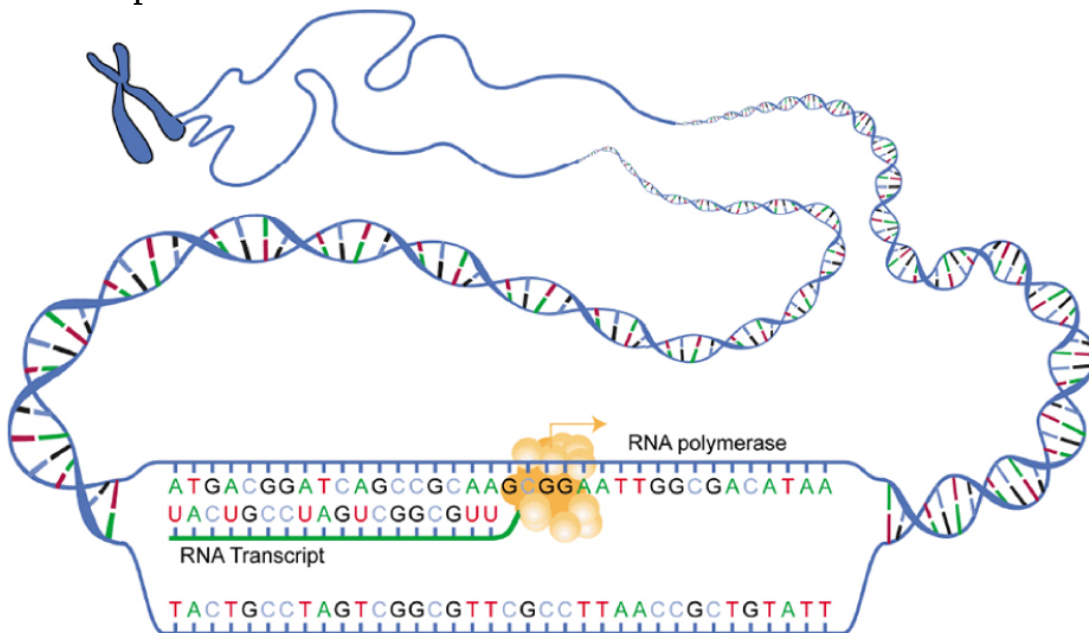
DNA is housed within the nucleus, and protein synthesis takes place in the cytoplasm, thus there must be some sort of intermediate messenger that leaves the nucleus and manages protein synthesis. This intermediate messenger is **messenger RNA (mRNA)**, a single-stranded nucleic acid that carries a copy of the genetic code for a single gene out of the nucleus and into the cytoplasm where it is used to produce proteins.

There are several different types of RNA, each having different functions in the cell. The structure of RNA is similar to DNA with a few small exceptions. For one thing, unlike DNA, most types of RNA, including

mRNA, are single-stranded and contain no complementary strand. Second, the ribose sugar in RNA contains an additional oxygen atom compared with DNA. Finally, instead of the base thymine, RNA contains the base uracil. This means that adenine will always pair up with uracil during the protein synthesis process.

Gene expression begins with the process called **transcription**, which is the synthesis of a strand of mRNA that is complementary to the gene of interest. This process is called transcription because the mRNA is like a transcript, or copy, of the gene's DNA code. Transcription begins in a fashion somewhat like DNA replication, in that a region of DNA unwinds and the two strands separate, however, only that small portion of the DNA will be split apart. The triplets within the gene on this section of the DNA molecule are used as the template to transcribe the complementary strand of RNA ([\[link\]](#)). A **codon** is a three-base sequence of mRNA, so-called because they directly encode amino acids. Like DNA replication, there are three stages to transcription: initiation, elongation, and termination.

Transcription: from DNA to mRNA



In the first of the two stages of making protein from DNA, a gene on the DNA molecule is transcribed into a complementary mRNA molecule.

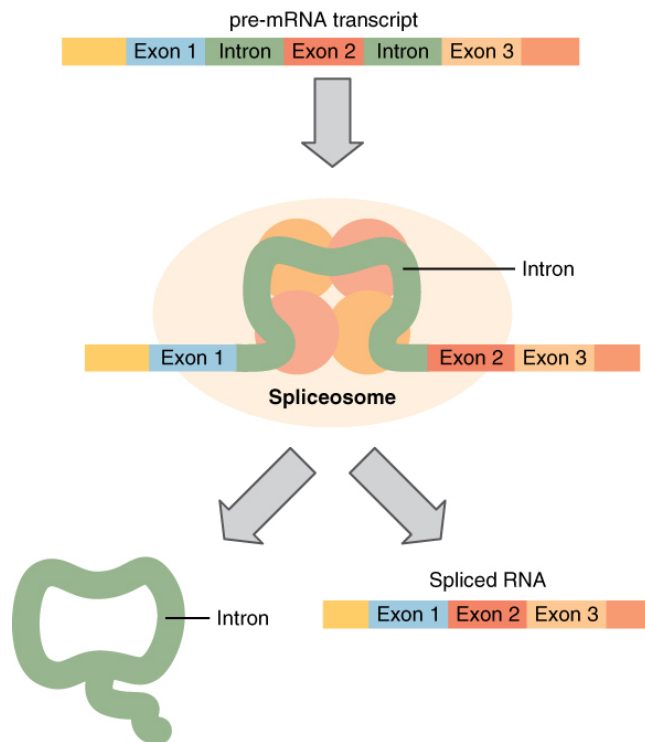
Stage 1: Initiation. A region at the beginning of the gene called a **promoter**—a particular sequence of nucleotides—triggers the start of transcription.

Stage 2: Elongation. Transcription starts when RNA polymerase unwinds the DNA segment. One strand, referred to as the coding strand, becomes the template with the genes to be coded. The polymerase then aligns the correct nucleic acid (A, C, G, or U) with its complementary base on the coding strand of DNA. **RNA polymerase** is an enzyme that adds new nucleotides to a growing strand of RNA. This process builds a strand of mRNA.

Stage 3: Termination. When the polymerase has reached the end of the gene, one of three specific triplets (UAA, UAG, or UGA) codes a “stop” signal, which triggers the enzymes to terminate transcription and release the mRNA transcript.

Before the mRNA molecule leaves the nucleus and proceeds to protein synthesis, it is modified in a number of ways. For this reason, it is often called a pre-mRNA at this stage. For example, your DNA, and thus complementary mRNA, contains long regions called non-coding regions that do not code for amino acids. Their function is still a mystery, but the process called **splicing** removes these non-coding regions from the pre-mRNA transcript ([\[link\]](#)). A **spliceosome**—a structure composed of various proteins and other molecules—attaches to the mRNA and “splices” or cuts out the non-coding regions. The removed segment of the transcript is called an **intron**. The remaining exons are pasted together. An **exon** is a segment of RNA that remains after splicing. Interestingly, some introns that are removed from mRNA are not always non-coding. When different coding regions of mRNA are spliced out, different variations of the protein will eventually result, with differences in structure and function. This process results in a much larger variety of possible proteins and protein functions. When the mRNA transcript is ready, it travels out of the nucleus and into the cytoplasm.

Splicing DNA



In the nucleus, a structure called a spliceosome cuts out introns (noncoding regions) within a pre-mRNA transcript and reconnects the exons.

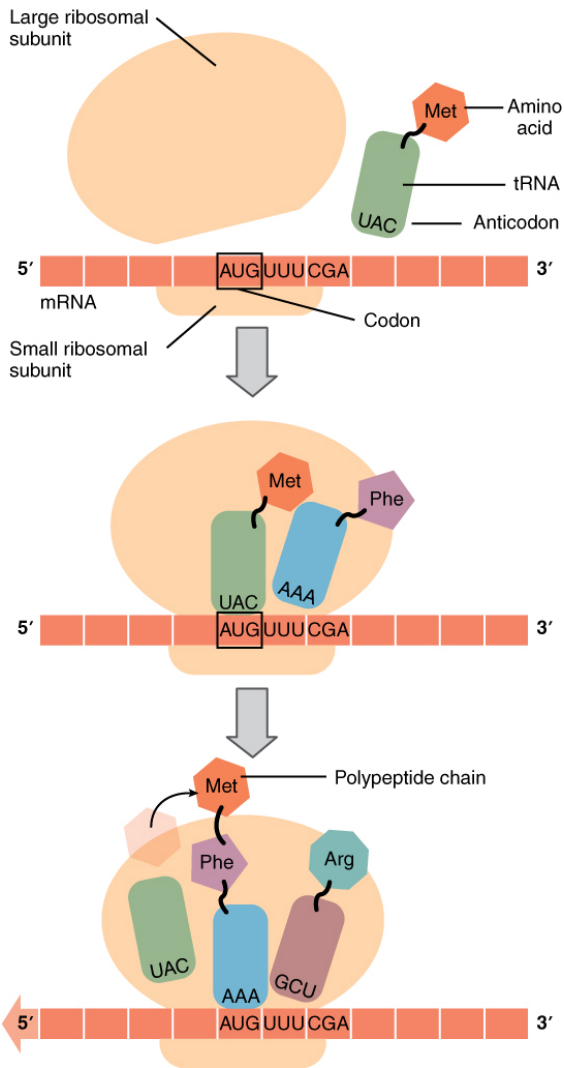
From RNA to Protein: Translation

Like translating a book from one language into another, the codons on a strand of mRNA must be translated into the amino acid alphabet of proteins. **Translation** is the process of synthesizing a chain of amino acids called a **polypeptide**. Translation requires two major aids: first, a “translator,” the molecule that will conduct the translation, and second, a substrate on which the mRNA strand is translated into a new protein, like the translator’s “desk.” Both of these requirements are fulfilled by other types of RNA. The substrate on which translation takes place is the ribosome.

Remember that many of a cell's ribosomes are found associated with the rough ER, and carry out the synthesis of proteins destined for the Golgi apparatus. **Ribosomal RNA (rRNA)** is a type of RNA that, together with proteins, composes the structure of the ribosome. Ribosomes exist in the cytoplasm as two distinct components, a small and a large subunit. When an mRNA molecule is ready to be translated, the two subunits come together and attach to the mRNA. The ribosome provides a substrate for translation, bringing together and aligning the mRNA molecule with the molecular “translators” that must decipher its code.

The other major requirement for protein synthesis is the translator molecules that physically “read” the mRNA codons. **Transfer RNA (tRNA)** is a type of RNA that ferries the appropriate corresponding amino acids to the ribosome, and attaches each new amino acid to the last, building the polypeptide chain one-by-one. Thus tRNA transfers specific amino acids from the cytoplasm to a growing polypeptide. The tRNA molecules must be able to recognize the codons on mRNA and match them with the correct amino acid. The tRNA is modified for this function. On one end of its structure is a binding site for a specific amino acid. On the other end is a base sequence that matches the codon specifying its particular amino acid. This sequence of three bases on the tRNA molecule is called an **anticodon**. For example, a tRNA responsible for shuttling the amino acid glycine contains a binding site for glycine on one end. On the other end it contains an anticodon that complements the glycine codon (GGA is a codon for glycine, and so the tRNAs anticodon would read CCU). Equipped with its particular cargo and matching anticodon, a tRNA molecule can read its recognized mRNA codon and bring the corresponding amino acid to the growing chain ([link](#)).

Translation from RNA to Protein



During translation, the mRNA transcript is “read” by a functional complex consisting of the ribosome and tRNA molecules. tRNAs bring the appropriate amino acids in sequence to the growing polypeptide chain by matching their anti-codons with codons on the mRNA strand.

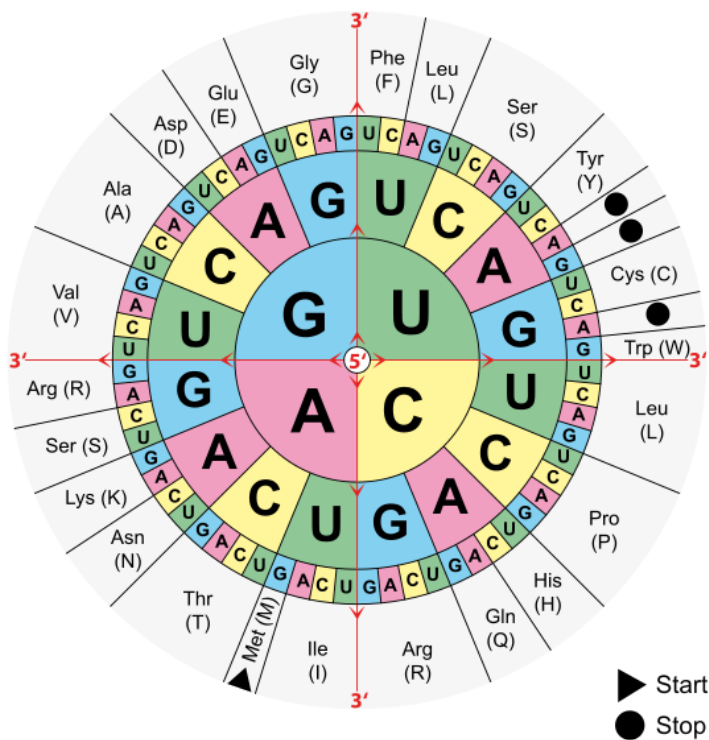
Commonly, an mRNA molecule will be translated simultaneously by several adjacent ribosomes. This increases the efficiency of protein synthesis. A single ribosome might translate an mRNA molecule in approximately one minute; so multiple ribosomes aboard a single transcript could produce multiple times the number of the same protein in the same minute. A **polyribosome** is a string of ribosomes translating a single mRNA strand.

Note:



Watch this [video](#) to learn about ribosomes. The ribosome binds to the mRNA molecule to start translation of its code into a protein. What happens to the small and large ribosomal subunits at the end of translation?

Translation works because each unique anticodon carries a specific amino acid. The same anticodon carries the same amino acid in virtually all living organisms on earth. This is why gene splicing and genetic engineering work. The complete collection of amino-acid/nucleotide-sequence relationships is called the **Genetic Code**. However, *the Genetic Code uses the complementary mRNA codon sequences rather than the tRNA anticodon sequences* to denote the relationship with the amino acid. The Genetic Code is presented in various formats. The two most common are the table format (not shown) and the wheel format shown below ([\[link\]](#)).
The Genetic Code



Genetic Code By Mouagip: Public domain,
via Wikimedia Commons

The wheel is read from the center out (in the 5' to 3' direction). It is read by finding the first letter of the codon sequence in the inner most circle, then finding the second letter of the codon sequence from the four choices next to it in the second ring. The process is repeated in the third ring by choosing the third letter of the codon sequence from the four choices next to the second letter. The amino acid associated with the codon is found in the adjacent segment outside the circle.

Notice that four of the codon sequences have special significance. The sequence AUG is the start codon. This tells the ribosome where to start the translation. It also codes for the amino acid methionine. The other three special codon sequences are, UAA, UAG, and UGA. These are the stop codons. When the ribosome encounters these codons it stops the translation and releases the newly formed protein.

Looking at the amino acids around the outside of the wheel you also should notice that while each codon sequence is specific to a single amino acid, the reverse is not true. Most of the amino acids are associated with more than one codon. This *redundancy* in the Genetic Code can have a significant effect in some circumstances. Point mutations can occur in the DNA where one base is substituted for another. Even though the DNA has a mutation, the sequence now is different, if the resulting mRNA codon still codes for the same amino acid the resulting protein will not change. When this happens it is called a *silent mutation*.

Gene Mutations

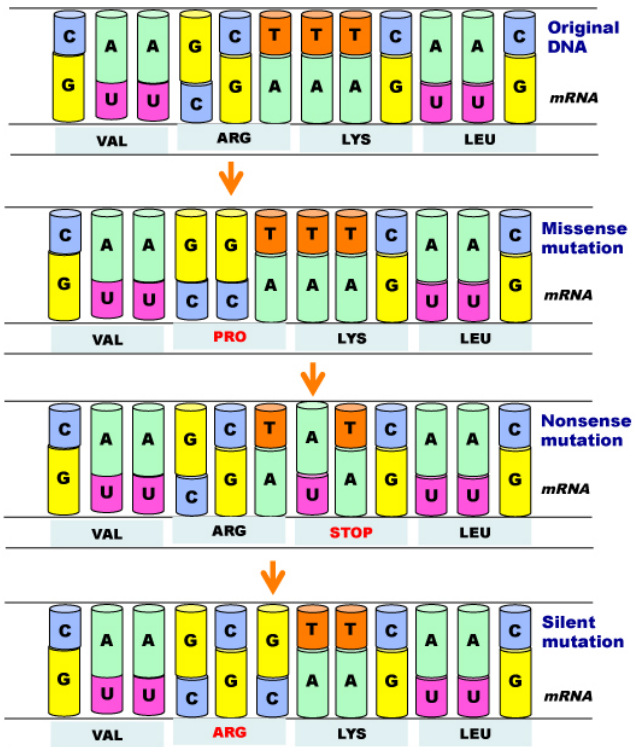
There are many ways the DNA can be altered by mutation. However, the changes to the original sequence are one of the three generic types:

- **Base Substitution:** where one base is replaced by another
- **Insertion:** where one or more bases are added to the sequence
- **Deletion:** where one or more bases are removed from the sequence

The effects of the mutation will differ depending on the specifics of each case. The effect generally will fall into one of four categories:

- **Missense:** where the mutation codes for a different amino acid at that location changing the resulting protein
- **Nonsense:** where the mutation codes for one of the three stop codons stopping the translation early
- **Silent:** where the DNA sequence changes but still codes for the same amino acid so the resulting protein is unchanged

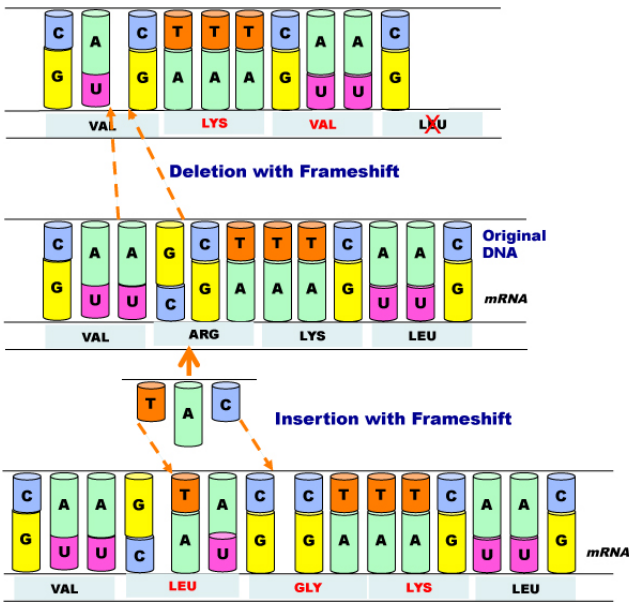
[\[link\]](#))



Effects From Single-Base Mutations

- **Frameshift:** where an insertion or deletion does not occur in a multiple of three bases or occurs in the middle of a triplet so it alters the reading frame and causes misreading of all the amino acids that follow

[[link](#)])



Examples of frameshift from insertions and deletions

The changes to the DNA can occur on a base-by-base basis. However, it also is common for some DNA segments to cause changes or mutations as a group. These are known as a transposable element or **Transposon**. This occurs both as *Chromosomal Rearrangement* on the same chromosome or as *Chromosomal Translocation* where the genetic material is exchanged between non-homologous chromosomes. Transposons tend to affect the coding in different ways than point mutations. They can affect gene expression in a number of ways.

A common gene element mutation is **Gene Duplication** where additional copies of a gene are inserted into the sequence during the replication process. The gene-repeats produced by this process can lead to additional expression of the gene which produces more of the protein in the body. Depending on the circumstance this may be beneficial or it may cause disease. It does not have to be the entire gene that duplicates. Sometimes only specific sequences within the gene are involved in the duplication. Huntington's disease is caused by a repeating section of the HTT gene. This section of the gene appears prone to duplication, at least in some

individuals. When the number of repeats of this segment hits a threshold the Huntingtin protein it produces is altered (misshapen) enough that it no longer functions properly.

Gene duplication also plays an important role in evolution. From an evolutionary perspective there can be an advantage to generating additional copies of a functioning gene. The additional copies provide raw material for modification while leaving other unchanged copies of the gene to produce the original protein necessary to carry out the normal physiological processes. Without extra copies this would not be possible and every new protein would have to evolve from scratch rather than from modification of an existing functional protein.

Another way transposons can affect outcomes is by changing gene expression that is controlled by specific promoters and inhibitors. When a transposon relocates it can change the relationship between the genes it carries and their promoters or inhibitors. Depending on where the transposon moves it may make previously inactive genes active or active genes inactive. The transposon also may have an effect on surrounding genes. If it inserts between an active gene and its promoter it may inactivate that gene. Additionally, if a transposon inserts at an intron/exon splicing boundary it can change the splicing characteristics and alter the protein variants produced.

Chapter Review

DNA stores the information necessary for instructing the cell to perform all of its functions. Cells use the genetic code stored within DNA to build proteins, which ultimately determine the structure and function of the cell. This genetic code lies in the particular sequence of nucleotides that make up each gene along the DNA molecule. To “read” this code, the cell must perform two sequential steps. In the first step, *transcription*, the DNA code is converted into a RNA code. A molecule of messenger RNA that is complementary to a specific gene is synthesized in a process similar to DNA replication. The molecule of mRNA provides the code to synthesize a protein. In the process of *translation*, the mRNA attaches to a ribosome. Next, tRNA molecules shuttle the appropriate amino acids to the ribosome,

one-by-one, coded by sequential triplet codons on the mRNA, until the protein is fully synthesized. When completed, the mRNA detaches from the ribosome, and the protein is released. Because the same codon is associated with the same amino acid in virtually all species a universal *Genetic Code* can be used to determine the amino acid sequence from any mRNA molecule. While each codon is associated with a single amino acid, the reverse is not true. Most amino acids have *redundancy*, meaning they are coded for by more than one codon. Typically, multiple ribosomes attach to a single mRNA molecule at once such that multiple proteins can be manufactured from the mRNA concurrently.

Interactive Link Questions

Exercise:

Problem:

Watch this [video](#) to learn about ribosomes. The ribosome binds to the mRNA molecule to start translation of its code into a protein. What happens to the small and large ribosomal subunits at the end of translation?

Solution:

They separate and move and are free to join translation of other segments of mRNA.

Review Questions

Exercise:

Problem:

Which of the following is *not* a difference between DNA and RNA?

- a. DNA contains thymine whereas RNA contains uracil
- b. DNA contains deoxyribose and RNA contains ribose

- c. DNA contains alternating sugar-phosphate molecules whereas RNA does not contain sugars
 - d. RNA is single stranded and DNA is double stranded
-

Solution:

C

Exercise:

Problem:

Transcription and translation take place in the _____ and _____, respectively.

- a. nucleus; cytoplasm
 - b. nucleolus; nucleus
 - c. nucleolus; cytoplasm
 - d. cytoplasm; nucleus
-

Solution:

A

Exercise:

Problem:

How many “letters” of an RNA molecule, in sequence, does it take to provide the code for a single amino acid?

- a. 1
 - b. 2
 - c. 3
 - d. 4
-

Solution:

C

Exercise:

Problem: Which of the following is *not* made out of RNA?

- a. the carriers that shuffle amino acids to a growing polypeptide strand
- b. the ribosome
- c. the messenger molecule that provides the code for protein synthesis
- d. the intron

Solution:

B

Critical Thinking Questions

Exercise:

Problem:

Briefly explain the similarities between transcription and DNA replication.

Solution:

Transcription and DNA replication both involve the synthesis of nucleic acids. These processes share many common features—particularly, the similar processes of initiation, elongation, and termination. In both cases the DNA molecule must be untwisted and separated, and the coding (i.e., sense) strand will be used as a template. Also, polymerases serve to add nucleotides to the growing DNA or mRNA strand. Both processes are signaled to terminate when completed.

Exercise:**Problem:**

Contrast transcription and translation. Name at least three differences between the two processes.

Solution:

Transcription is really a “copy” process and translation is really an “interpretation” process, because transcription involves copying the DNA message into a very similar RNA message whereas translation involves converting the RNA message into the very different amino acid message. The two processes also differ in their location: transcription occurs in the nucleus and translation in the cytoplasm. The mechanisms by which the two processes are performed are also completely different: transcription utilizes polymerase enzymes to build mRNA whereas translation utilizes different kinds of RNA to build protein.

Exercise:**Problem:**

Briefly explain what a silent mutation is and why it can happen.

Solution:

A silent mutation is a base substitution in the DNA sequence that, while different from the original, still codes for that same amino acid. This can happen because of the redundancy in the Genetic Code. While a given codon always codes for a specific amino acid, other codons may also code for that same amino acid. Codons that code for the same amino acid usually differ by only one base in their codon triplet. This means if a mutation happens at this location there is at least a one in three chance that it will also code for the same amino acid in the same place and there will be no change in the resulting protein.

Glossary

anticodon

consecutive sequence of three nucleotides on a tRNA molecule that is complementary to a specific codon on an mRNA molecule

codon

consecutive sequence of three nucleotides on an mRNA molecule that corresponds to a specific amino acid

exon

one of the coding regions of an mRNA molecule that remain after splicing

gene

functional length of DNA that provides the genetic information necessary to build a protein

gene expression

active interpretation of the information coded in a gene to produce a functional gene product

intron

non-coding regions of a pre-mRNA transcript that may be removed during splicing

messenger RNA (mRNA)

nucleotide molecule that serves as an intermediate in the genetic code between DNA and protein

polypeptide

chain of amino acids linked by peptide bonds

polyribosome

simultaneous translation of a single mRNA transcript by multiple ribosomes

promoter

region of DNA that signals transcription to begin at that site within the gene

proteome

full complement of proteins produced by a cell (determined by the cell's specific gene expression)

ribosomal RNA (rRNA)

RNA that makes up the subunits of a ribosome

RNA polymerase

enzyme that unwinds DNA and then adds new nucleotides to a growing strand of RNA for the transcription phase of protein synthesis

spliceosome

complex of enzymes that serves to splice out the introns of a pre-mRNA transcript

splicing

the process of modifying a pre-mRNA transcript by removing certain, typically non-coding, regions

transcription

process of producing an mRNA molecule that is complementary to a particular gene of DNA

transfer RNA (tRNA)

molecules of RNA that serve to bring amino acids to a growing polypeptide strand and properly place them into the sequence

translation

process of producing a protein from the nucleotide sequence code of an mRNA transcript

triplet

consecutive sequence of three nucleotides on a DNA molecule that, when transcribed into an mRNA codon, corresponds to a particular amino acid

Bis2A 14.0 Regulation of Gene Expression Overview

By the end of this section, you will be able to:

- Discuss why every cell does not express all of its genes
- Describe how prokaryotic gene regulation occurs at the transcriptional level
- Discuss how eukaryotic gene regulation occurs at the epigenetic, transcriptional, post-transcriptional, translational, and post-translational levels

For a cell to function properly, necessary proteins must be synthesized at the proper time. All cells control or regulate the synthesis of proteins from information encoded in their DNA. The process of turning on a gene to produce RNA and protein is called **gene expression**. Whether in a simple unicellular organism or a complex multi-cellular organism, each cell controls when and how its genes are expressed. For this to occur, there must be a mechanism to control when a gene is expressed to make RNA and protein, how much of the protein is made, and when it is time to stop making that protein because it is no longer needed.

The regulation of gene expression conserves energy and space. It would require a significant amount of energy for an organism to express every gene at all times, so it is more energy efficient to turn on the genes only when they are required. In addition, only expressing a subset of genes in each cell saves space because DNA must be unwound from its tightly coiled structure to transcribe and translate the DNA. Cells would have to be enormous if every protein were expressed in every cell all the time.

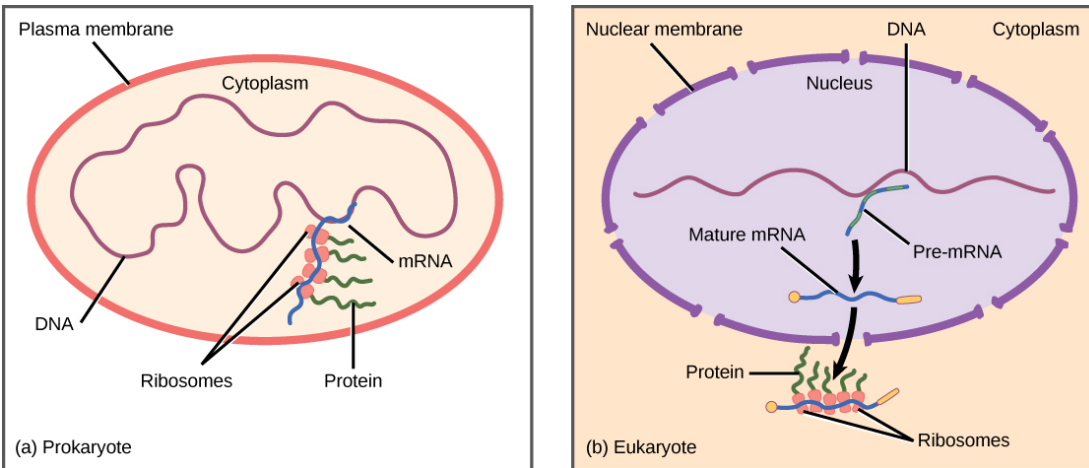
The control of gene expression is extremely complex. Malfunctions in this process are detrimental to the cell and can lead to the development of many diseases, including cancer.

Prokaryotic versus Eukaryotic Gene Expression

To understand how gene expression is regulated, we must first understand how a gene codes for a functional protein in a cell. The process occurs in both prokaryotic and eukaryotic cells, just in slightly different manners.

Prokaryotic organisms are single-celled organisms that lack a cell nucleus, and their DNA therefore floats freely in the cell cytoplasm. To synthesize a protein, the processes of transcription and translation occur almost simultaneously. When the resulting protein is no longer needed, transcription stops. As a result, the primary method to control what type of protein and how much of each protein is expressed in a prokaryotic cell is the regulation of DNA transcription. All of the subsequent steps occur automatically. When more protein is required, more transcription occurs. Therefore, in prokaryotic cells, the control of gene expression is mostly at the transcriptional level.

Eukaryotic cells, in contrast, have intracellular organelles that add to their complexity. In eukaryotic cells, the DNA is contained inside the cell's nucleus and there it is transcribed into RNA. The newly synthesized RNA is then transported out of the nucleus into the cytoplasm, where ribosomes translate the RNA into protein. The processes of transcription and translation are physically separated by the nuclear membrane; transcription occurs only within the nucleus, and translation occurs only outside the nucleus in the cytoplasm. The regulation of gene expression can occur at all stages of the process ([\[link\]](#)). Regulation may occur when the DNA is uncoiled and loosened from nucleosomes to bind transcription factors (**epigenetic** level), when the RNA is transcribed (transcriptional level), when the RNA is processed and exported to the cytoplasm after it is transcribed (**post-transcriptional** level), when the RNA is translated into protein (translational level), or after the protein has been made (**post-translational** level).



Prokaryotic transcription and translation occur simultaneously in the cytoplasm, and regulation occurs at the transcriptional level. Eukaryotic gene expression is regulated during transcription and RNA processing, which take place in the nucleus, and during protein translation, which takes place in the cytoplasm. Further regulation may occur through post-translational modifications of proteins.

The differences in the regulation of gene expression between prokaryotes and eukaryotes are summarized in [\[link\]](#). The regulation of gene expression is discussed in detail in subsequent modules.

Differences in the Regulation of Gene Expression of Prokaryotic and Eukaryotic Organisms	
Prokaryotic organisms	Eukaryotic organisms
Lack nucleus	Contain nucleus

Differences in the Regulation of Gene Expression of Prokaryotic and Eukaryotic Organisms	
Prokaryotic organisms	Eukaryotic organisms
DNA is found in the cytoplasm	DNA is confined to the nuclear compartment
RNA transcription and protein formation occur almost simultaneously	RNA transcription occurs prior to protein formation, and it takes place in the nucleus. Translation of RNA to protein occurs in the cytoplasm.
Gene expression is regulated primarily at the transcriptional level	Gene expression is regulated at many levels (epigenetic, transcriptional, nuclear shuttling, post-transcriptional, translational, and post-translational)

Note:

Evolution Connection

Evolution of Gene Regulation

Prokaryotic cells can only regulate gene expression by controlling the amount of transcription. As eukaryotic cells evolved, the complexity of the control of gene expression increased. For example, with the evolution of eukaryotic cells came compartmentalization of important cellular components and cellular processes. A nuclear region that contains the DNA was formed. Transcription and translation were physically separated into two different cellular compartments. It therefore became possible to control gene expression by regulating transcription in the nucleus, and also by controlling the RNA levels and protein translation present outside the nucleus.

Some cellular processes arose from the need of the organism to defend itself. Cellular processes such as gene silencing developed to protect the cell from viral or parasitic infections. If the cell could quickly shut off gene expression for a short period of time, it would be able to survive an infection when other organisms could not. Therefore, the organism evolved a new process that helped it survive, and it was able to pass this new development to offspring.

Section Summary

While all somatic cells within an organism contain the same DNA, not all cells within that organism express the same proteins. Prokaryotic organisms express the entire DNA they encode in every cell, but not necessarily all at the same time. Proteins are expressed only when they are needed.

Eukaryotic organisms express a subset of the DNA that is encoded in any given cell. In each cell type, the type and amount of protein is regulated by controlling gene expression. To express a protein, the DNA is first transcribed into RNA, which is then translated into proteins. In prokaryotic cells, these processes occur almost simultaneously. In eukaryotic cells, transcription occurs in the nucleus and is separate from the translation that occurs in the cytoplasm. Gene expression in prokaryotes is regulated only at the transcriptional level, whereas in eukaryotic cells, gene expression is regulated at the epigenetic, transcriptional, post-transcriptional, translational, and post-translational levels.

Review Questions

Exercise:

Problem:

Control of gene expression in eukaryotic cells occurs at which level(s)?

- a. only the transcriptional level
- b. epigenetic and transcriptional levels

- c. epigenetic, transcriptional, and translational levels
 - d. epigenetic, transcriptional, post-transcriptional, translational, and post-translational levels
-

Solution:

D

Exercise:

Problem: Post-translational control refers to:

- a. regulation of gene expression after transcription
 - b. regulation of gene expression after translation
 - c. control of epigenetic activation
 - d. period between transcription and translation
-

Solution:

B

Free Response

Exercise:

Problem:

Name two differences between prokaryotic and eukaryotic cells and how these differences benefit multicellular organisms.

Solution:

Eukaryotic cells have a nucleus, whereas prokaryotic cells do not. In eukaryotic cells, DNA is confined within the nuclear region. Because of this, transcription and translation are physically separated. This creates a more complex mechanism for the control of gene expression

that benefits multicellular organisms because it compartmentalizes gene regulation.

Gene expression occurs at many stages in eukaryotic cells, whereas in prokaryotic cells, control of gene expression only occurs at the transcriptional level. This allows for greater control of gene expression in eukaryotes and more complex systems to be developed. Because of this, different cell types can arise in an individual organism.

Exercise:

Problem:

Describe how controlling gene expression will alter the overall protein levels in the cell.

Solution:

The cell controls which proteins are expressed and to what level each protein is expressed in the cell. Prokaryotic cells alter the transcription rate to turn genes on or off. This method will increase or decrease protein levels in response to what is needed by the cell. Eukaryotic cells change the accessibility (epigenetic), transcription, or translation of a gene. This will alter the amount of RNA and the lifespan of the RNA to alter the amount of protein that exists. Eukaryotic cells also control protein translation to increase or decrease the overall levels. Eukaryotic organisms are much more complex and can manipulate protein levels by changing many stages in the process.

Glossary

epigenetic

heritable changes that do not involve changes in the DNA sequence

gene expression

processes that control the turning on or turning off of a gene

post-transcriptional

control of gene expression after the RNA molecule has been created
but before it is translated into protein

post-translational

control of gene expression after a protein has been created

Bis2A 14.1 Bacterial Gene Regulation

By the end of this section, you will be able to:

- Describe the steps involved in prokaryotic gene regulation
- Explain the roles of activators, inducers, and repressors in gene regulation

The DNA of bacteria and archaea is usually (there are a few known exceptions to the circular chromosome in bacteria) organized into a circular chromosome supercoiled in the nucleoid region of the cell cytoplasm. Proteins that are needed for a specific function, or that are involved in the same biochemical pathway, are often times encoded together in blocks called **operons**. Therefore, operons are single transcription units, encoding for multiple genes. Expression of these genes is organized from a single regulatory region and all genes in the operon are therefore regulated as a single unit. For example, all of the genes needed to use lactose as an energy source are coded next to each other in the lactose (or *lac*) operon.

In bacteria, all transcription is controlled through RNA polymerase, a multiprotein complex that recognizes the promoter region and initiates transcription, elongates the transcript, and terminates transcription. Therefore, gene expression can be regulated at any of these steps, initiation, elongation, or termination; however, in bacteria, the majority of the regulation is at the level of transcription initiation.

The Role of the Promoter

The first level of control of gene expression is at the promoter itself. There are two ways a promoter controls gene expression. First is which RNA polymerase holoenzyme (sigma + Core RNA polymerase) recognizes the promoter. Remember, bacteria have a number of sigma factors many of which control gene expression only under certain conditions, such as Sigma-S during stationary phase. The second level of control is promoter strength, some promoters are considered "strong", while others are considered "weak". The basis of promoter strength is the specificity the promoter has to RNA polymerase. Each different sigma factor has a different recognition sequence, for example, the sigma-70 protein in *E. coli* has the recognition sequence 5'-TTGACA-(16-17 nucleotides)-TATAAT-3'.

Strong promoters have sequences close to the consensus recognition sequence, weak promoters have sequences more divergent to the consensus.

Regulator Proteins

The next layer of control is the addition of **regulatory** proteins. These proteins can either act to increase transcription, and are often called **activators** or **activator proteins**. These proteins bind to the promoter region and aid RNA polymerase to recognize a promoter and initiate transcription. Alternatively, regulatory proteins that inhibit transcription are often referred to as **repressors** or **repressor proteins**. Some regulatory proteins can act both as a repressor or an activator depending upon how they interact with RNA polymerase and the promoter. For example the regulatory protein called CAP can act to activate some genes and repress other genes. Therefore the terms "activator" and "repressor" should be used depending upon the situation or condition, and may not truly reflect the role of the protein in question.

Allosteric modulators of Protein Regulators

Many regulatory proteins do not function independently, instead they rely on an allosteric regulatory molecule to control their activity. These small molecules are often referred to as **inducers** or **co-repressors** or **co-activators**. These small molecules are often metabolites, such as lactose or tryptophan or small regulatory molecules, such as cAMP or GTP. Below are some examples of regulatory systems that are controlled by repression and by activation. In some instances the presence of the small molecule activates or enhances the DNA-binding activity of the protein, thereby allowing the protein to bind better and regulate (either activate or repress) transcription initiation. Alternatively, the small molecule interacts with the regulatory protein and inhibits or decreases its ability to interact with the DNA or RNA polymerase, which can lead to either activation or repression of the gene it is controlling.

Repressors vs Activators: How do you tell

Expression of the gene

In general there are three states that can be used to describe the expression of a gene or operon. The first is **constitutive**. That the level of expression

observed under most conditions. This level of expression could be very high, if the promoter is strong, or expression could be very little, if the promoter is weak. Regardless of the amount of expression, we observe very little change in expression under a variety of conditions. The second state is **activation** or **induction**, that is under a specific set of conditions, the expression of a gene or operon is increased or activated. Finally, expression of a gene can be decreased under a certain set of conditions, this is called **repression**. Mechanistically, in the last two cases, regulatory proteins are required to change the constitutive expression pattern. Whether a regulatory protein acts in a positive way, that is as an activator or acts in a negative way, as a repressor is not necessarily obvious.

A simple test

So how does one determine if a regulatory protein functions in a positive or negative way? A simple genetic test is to ask "what happens to expression if the regulatory protein is absent?" If a regulatory protein is acting positively, then its presence is required to activate gene expression. In its absence, there is no regulatory protein, therefore no activation, and the outcome is no transcription. The phenotype of a null mutation in a regulatory protein is no activation. The opposite is true for a regulatory protein acting negatively. In its absence expression should be increased, because the gene keeping expression low is no longer around.

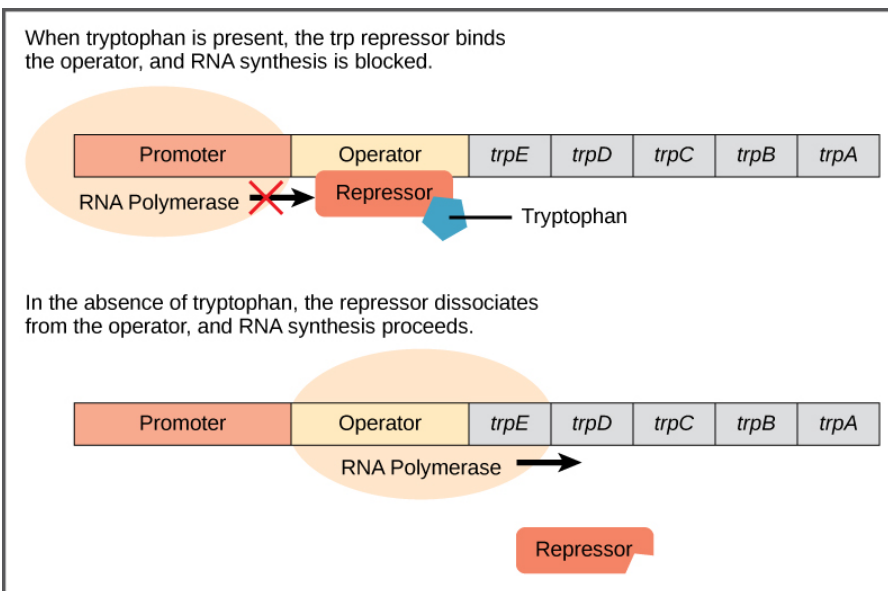
Repression vs Activation

What should become clear, is that how a regulatory protein functions: negatively or positively, may be independent as to what its effect is on gene expression. As you will see below, when *E. coli* is grown in the presence of lactose (and in the absence of glucose) expression of the *lac* operon is induced or activated. Yet, the protein regulator that is responsible for this expression phenotype is a repressor; it binds to the DNA to prevent transcription and a null mutation that removes the gene (*lacI*) increases expression of the *lac* operon. In other words, the mechanism by which a regulatory protein works (positively or negatively) is independent as to how the gene or operon is expressed and behaves. This apparent contradiction can be rationalized when you incorporate the role of the allosteric regulator; in this case lactose. As you will see in the examples below, the key to the

regulation is two fold: the mechanism by which the regulator works and the role and nature of the allosteric regulator.

The *trp* Operon: A Repressor Operon

Bacteria such as *E. coli* need amino acids to survive. **Tryptophan** is one such amino acid that *E. coli* can ingest from the environment. *E. coli* can also synthesize tryptophan using enzymes that are encoded by five genes. These five genes are next to each other in what is called the **tryptophan (*trp*) operon** ([\[link\]](#)). If tryptophan is present in the environment, then *E. coli* does not need to synthesize it and the switch controlling the activation of the genes in the *trp* operon is switched off. However, when tryptophan availability is low, the switch controlling the operon is turned on, transcription is initiated, the genes are expressed, and tryptophan is synthesized.



The five genes that are needed to synthesize tryptophan in *E. coli* are located next to each other in the *trp* operon. When tryptophan is plentiful, two tryptophan molecules bind the repressor protein at the operator sequence. This physically

blocks the RNA polymerase from transcribing the tryptophan genes. When tryptophan is absent, the repressor protein does not bind to the operator and the genes are transcribed.

A DNA sequence that codes for proteins is referred to as the coding region. The five coding regions for the tryptophan biosynthesis enzymes are arranged sequentially on the chromosome in the operon. Just before the coding region is the **transcriptional start site**. This is the region of DNA to which RNA polymerase binds to initiate transcription. The promoter sequence is upstream of the transcriptional start site; each operon has a sequence within or near the promoter to which proteins (activators or repressors) can bind and regulate transcription.

A DNA sequence called the operator sequence is encoded between the promoter region and the first *trp* coding gene. This **operator** contains the DNA code to which the repressor protein can bind. When tryptophan is present in the cell, two tryptophan molecules bind to the *trp* repressor, which changes shape to bind to the *trp* operator. Binding of the tryptophan–repressor complex at the operator physically prevents the RNA polymerase from binding, and transcribing the downstream genes. It should be noted that the term "operator" is limited to just a few systems and almost always refers to the binding site for a repressor. Conceptually what you need to remember is that there are sites on the DNA that interact with regulatory proteins allowing them to perform their appropriate function, repress transcription or activate transcription. These regulatory protein binding sites can vary as to location, but all control or regulate how RNA polymerase initiates transcription.

When tryptophan is not present in the cell, the repressor by itself does not bind to the operator; therefore, the operon is active and tryptophan is synthesized. Because the repressor protein actively binds to the operator to keep the genes turned off, the *trp* operon is negatively regulated and the proteins that bind to the operator to silence *trp* expression are **negative regulators**.

Note:

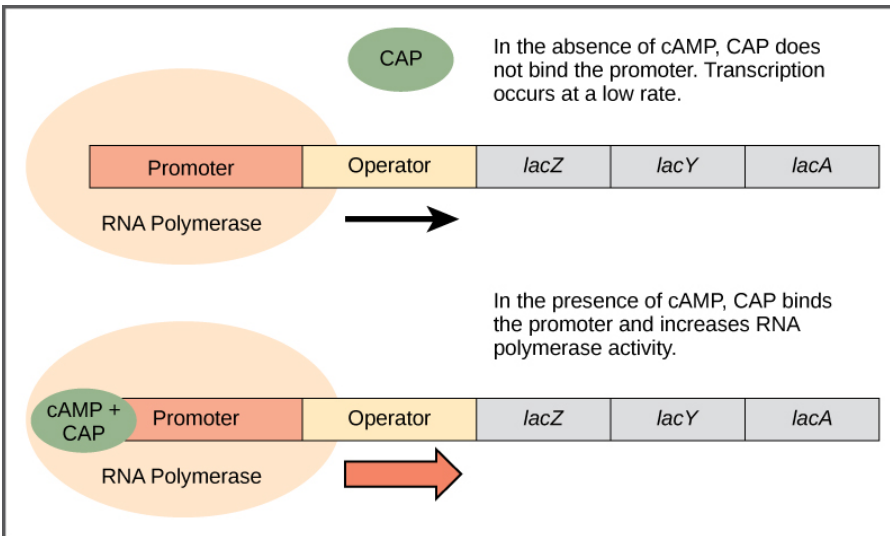
Link to Learning



Watch [this video](#) to learn more about the *trp* operon.

Catabolite Activator Protein (CAP): An Activator Regulator

Just as the *trp* operon is negatively regulated by tryptophan molecules, there are proteins that bind to the operator sequences that act as a **positive regulator** to turn genes on and activate them. For example, when glucose is scarce, *E. coli* bacteria can turn to other sugar sources for fuel. To do this, new genes to process these alternate genes must be transcribed. When glucose levels drop, cyclic AMP (cAMP) begins to accumulate in the cell. The cAMP molecule is a signaling molecule that is involved in glucose and energy metabolism in *E. coli*. When glucose levels decline in the cell, accumulating cAMP binds to the positive regulator **catabolite activator protein (CAP)**, a protein that binds to the promoters of operons that control the processing of alternative sugars. When cAMP binds to CAP, the complex binds to the promoter region of the genes that are needed to use the alternate sugar sources ([link](#)). In these operons, a CAP binding site is located upstream of the RNA polymerase binding site in the promoter. This increases the binding ability of RNA polymerase to the promoter region and the transcription of the genes. Please note, CAP-cAMP complex can also act as a repressor, depending upon where the binding site for CAP-cAMP is located. In the case of the Lactose operon, its position allows it to act as an activator; but in other operons it is positioned 3' or downstream from the promoter and can act as a repression.



When glucose levels fall, *E. coli* may use other sugars for fuel but must transcribe new genes to do so. As glucose supplies become limited, cAMP levels increase. This cAMP binds to the CAP protein, a positive regulator that binds to an operator region upstream of the genes required to use other sugar sources.

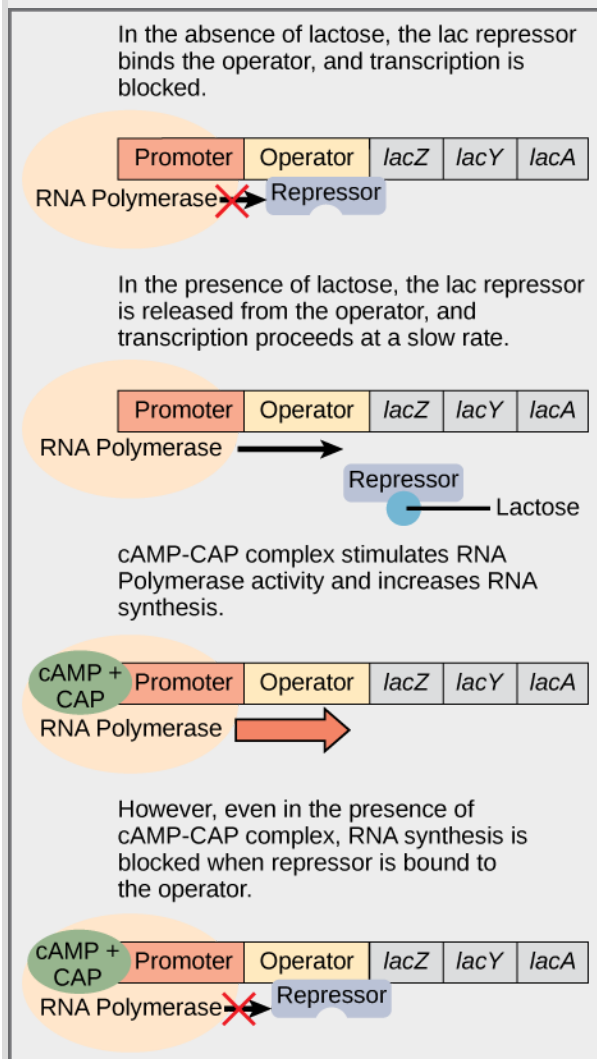
The *lac* Operon: An Inducer Operon

The third type of gene regulation in prokaryotic cells occurs through **inducible operons**, which have proteins that bind to activate or repress transcription depending on the local environment and the needs of the cell. The *lac* operon is a typical inducible operon. As mentioned previously, *E. coli* is able to use other sugars as energy sources when glucose concentrations are low. To do so, the cAMP–CAP protein complex serves as a positive regulator to induce transcription. One such sugar source is lactose. The ***lac* operon** encodes the genes necessary to acquire and process the lactose from the local environment. CAP binds to the operator sequence upstream of the promoter that initiates transcription of the *lac* operon. However, for the *lac* operon to be activated, two conditions must be met. First, the level of glucose must be very low or non-existent. Second, lactose

must be present. Only when glucose is absent and lactose is present will the *lac* operon be transcribed ([link](#)). This makes sense for the cell, because it would be energetically wasteful to create the proteins to process lactose if glucose was plentiful or lactose was not available.

Note:

Art Connection



Transcription of the *lac* operon is carefully regulated so that its expression only occurs when glucose is limited and lactose is

present to serve as an alternative fuel source.

In *E. coli*, the *trp* operon is on by default, while the *lac* operon is off. Why do you think this is the case?

If glucose is absent, then CAP can bind to the operator sequence to activate transcription. If lactose is absent, then the repressor binds to the operator to prevent transcription. If either of these requirements is met, then transcription remains off. Only when both conditions are satisfied is the *lac* operon transcribed ([link](#)).

Signals that Induce or Repress Transcription of the <i>lac</i> Operon				
Glucose	CAP binds	Lactose	Repressor binds	Transcription
+	-	-	+	No
+	-	+	-	Some
-	+	-	+	No
-	+	+	-	Yes

Note:

Link to Learning



Watch an [animated tutorial](#) about the workings of *lac* operon here.

Section Summary

The regulation of gene expression in prokaryotic cells occurs at the transcriptional level. There are three ways to control the transcription of an operon: repressive control, activator control, and inducible control.

Repressive control, typified by the *trp* operon, uses proteins bound to the operator sequence to physically prevent the binding of RNA polymerase and the activation of transcription. Therefore, if tryptophan is not needed, the repressor is bound to the operator and transcription remains off.

Activator control, typified by the action of CAP, increases the binding ability of RNA polymerase to the promoter when CAP is bound. In this case, low levels of glucose result in the binding of cAMP to CAP. CAP then binds the promoter, which allows RNA polymerase to bind to the promoter better. In the last example—the *lac* operon—two conditions must be met to initiate transcription. Glucose must not be present, and lactose must be available for the *lac* operon to be transcribed. If glucose is absent, CAP binds to the operator. If lactose is present, the repressor protein does not bind to its operator. Only when both conditions are met will RNA polymerase bind to the promoter to induce transcription.

Art Connections

Exercise:

Problem:

[\[link\]](#) In *E. coli*, the *trp* operon is on by default, while the *lac* operon is off. Why do you think that this is the case?

Solution:

[\[link\]](#) Tryptophan is an amino acid essential for making proteins, so the cell always needs to have some on hand. However, if plenty of tryptophan is present, it is wasteful to make more, and the expression of the *trp* receptor is repressed. Lactose, a sugar found in milk, is not always available. It makes no sense to make the enzymes necessary to digest an energy source that is not available, so the *lac* operon is only turned on when lactose is present.

Review Questions**Exercise:****Problem:**

If glucose is absent, but so is lactose, the *lac* operon will be _____.

- a. activated
- b. repressed
- c. activated, but only partially
- d. mutated

Solution:

B

Exercise:**Problem:**

Bacteria and archaea lack a nucleus. Therefore, the genes in bacteria and archaea are:

- a. all expressed, all of the time
- b. transcribed and translated almost simultaneously

- c. transcriptionally controlled because translation begins before transcription ends
 - d. b and c are both true
-

Solution:

D

Free Response

Exercise:

Problem:

Describe how transcription in bacteria can be altered by external stimulation such as excess lactose in the environment.

Solution:

Environmental stimuli can increase or induce transcription in bacteria. In this example, lactose in the environment will induce the transcription of the *lac* operon, but only if glucose is not available in the environment.

Exercise:

Problem:

What is the difference between a repressible and an inducible operon?

Solution:

A repressible operon uses a protein bound to the promoter region of a gene to keep the gene repressed or silent. This repressor must be actively removed in order to transcribe the gene. An inducible operon is either activated or repressed depending on the needs of the cell and what is available in the local environment.

Exercise: Exercise 6

Problem:

In the *lac* operon detailed above, LacI acts as a repressor and its allosteric regulator, lactose, acts as an inducer of the system. Redesign the *lacI* gene such that it no longer acts as a repressor but instead acts as an activator. What basic properties of the protein would need to change?

Solution:

First the *Lac* promoter would need to be much weaker promoter. Second, the LacI binding site (operator) would most likely need to move to the 5' end of the promoter. Third, when LacI binds to lactose, instead of decreasing the affinity of the protein to the DNA, it would need to increase the binding affinity. Similar to the way CAP-cAMP enhances the binding of CAP. In this hypothetical model, in the presence of lactose, lactose would bind LacI, cause a confirmation change that now stimulates LacI to bind to the promoter region and activate transcription. Hence, the expression pattern would look identical to as it does in the example above, except the mechanism of action by the regulator has changed from negative to positive.

Glossary

activator

protein that binds to prokaryotic operators to increase transcription

catabolite activator protein (CAP)

protein that complexes with cAMP to bind to the promoter sequences of operons that control sugar processing when glucose is not available

inducible operon

operon that can be activated or repressed depending on cellular needs and the surrounding environment

lac operon

operon in prokaryotic cells that encodes genes required for processing and intake of lactose

negative regulator

protein that prevents transcription

operator

region of DNA outside of the promoter region that binds activators or repressors that control gene expression in prokaryotic cells

operon

collection of genes involved in a pathway that are transcribed together as a single mRNA in prokaryotic cells

positive regulator

protein that increases transcription

repressor

protein that binds to the operator of prokaryotic genes to prevent transcription

transcriptional start site

site at which transcription begins

trp operon

series of genes necessary to synthesize tryptophan in prokaryotic cells

tryptophan

amino acid that can be synthesized by prokaryotic cells when necessary

Bis2A 14.2 Eukaryotic Epigenetic Gene Regulation

By the end of this section, you will be able to:

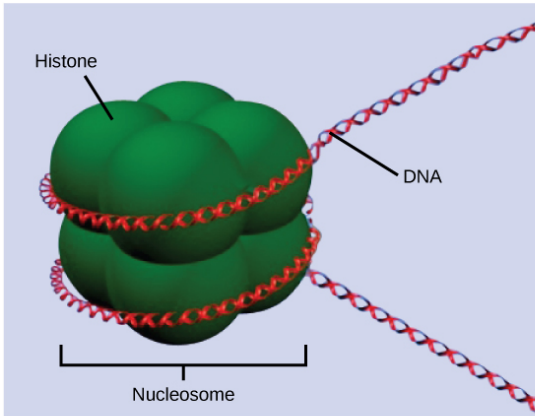
- Explain the process of epigenetic regulation
- Describe how access to DNA is controlled by histone modification

Eukaryotic gene expression is more complex than bacterial gene expression because the processes of transcription and translation are physically separated. Unlike bacteria or archaea, eukaryotic cells can regulate gene expression at many different levels. Eukaryotic gene expression begins with control of access to the DNA. This form of regulation, called epigenetic regulation, occurs even before transcription is initiated.

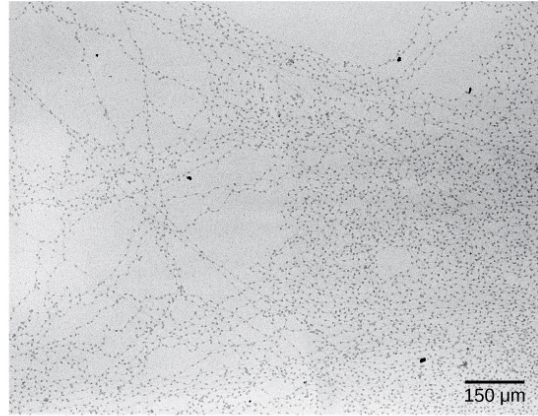
Epigenetic Control: Regulating Access to Genes within the Chromosome

The human genome encodes over 20,000 genes; each of the 23 pairs of human chromosomes encodes thousands of genes. The DNA in the nucleus is precisely wound, folded, and compacted into chromosomes so that it will fit into the nucleus. It is also organized so that specific segments can be accessed as needed by a specific cell type.

The first level of organization, or packing, is the winding of DNA strands around histone proteins. Histones package and order DNA into structural units called nucleosome complexes, which can control the access of proteins to the DNA regions ([\[link\]](#)**a**). Under the electron microscope, this winding of DNA around histone proteins to form nucleosomes looks like small beads on a string ([\[link\]](#)**b**). These beads (histone proteins) can move along the string (DNA) and change the structure of the molecule.



(a)



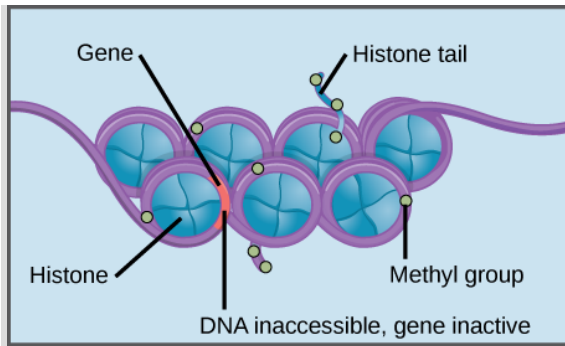
(b)

DNA is folded around histone proteins to create (a) nucleosome complexes. These nucleosomes control the access of proteins to the underlying DNA. When viewed through an electron microscope (b), the nucleosomes look like beads on a string. (credit “micrograph”: modification of work by Chris Woodcock)

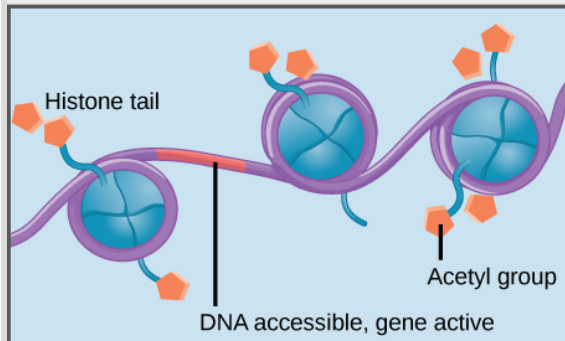
If DNA encoding a specific gene is to be transcribed into RNA, the nucleosomes surrounding that region of DNA can slide down the DNA to open that specific chromosomal region and allow for the transcriptional machinery (RNA polymerase) to initiate transcription ([\[link\]](#)). Nucleosomes can move to open the chromosome structure to expose a segment of DNA, but do so in a very controlled manner.

Note:

Art Connection



Methylation of DNA and histones causes nucleosomes to pack tightly together. Transcription factors cannot bind the DNA, and genes are not expressed.



Histone acetylation results in loose packing of nucleosomes. Transcription factors can bind the DNA and genes are expressed.

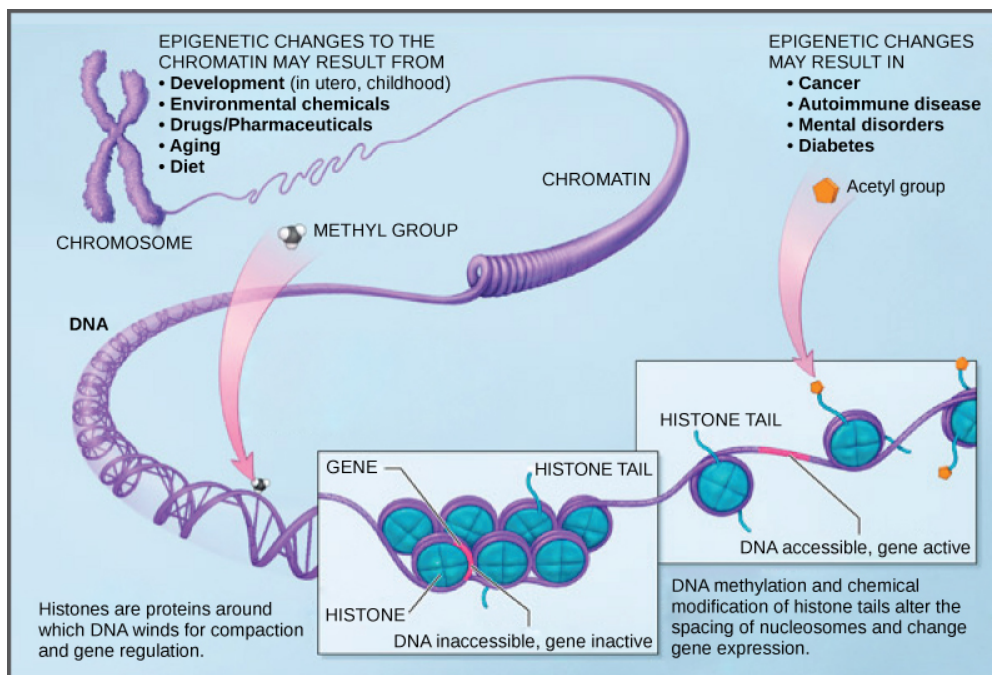
Nucleosomes can slide along DNA. When nucleosomes are spaced closely together (top), transcription factors cannot bind and gene expression is turned off. When the nucleosomes are spaced far apart (bottom), the DNA is exposed. Transcription factors can bind, allowing gene expression to occur. Modifications to the histones and DNA affect nucleosome spacing.

In females, one of the two X chromosomes is inactivated during embryonic development because of epigenetic changes to the chromatin. What impact do you think these changes would have on nucleosome packing?

How the histone proteins move is dependent on signals found on both the histone proteins and on the DNA. These signals are tags added to histone proteins and DNA that tell the histones if a chromosomal region should be open or closed ([link](#) depicts modifications to histone proteins and DNA). These tags are not permanent, but may be added or removed as needed.

They are chemical modifications (phosphate, methyl, or acetyl groups) that are attached to specific amino acids in the protein or to the nucleotides of the DNA. The tags do not alter the DNA base sequence, but they do alter how tightly wound the DNA is around the histone proteins. DNA is a negatively charged molecule; therefore, changes in the charge of the histone will change how tightly wound the DNA molecule will be. When unmodified, the histone proteins have a large positive charge; by adding chemical modifications like acetyl groups, the charge becomes less positive.

The DNA molecule itself can also be modified. This occurs within very specific regions called CpG islands. These are stretches with a high frequency of cytosine and guanine dinucleotide DNA pairs (CG) found in the promoter regions of genes. When this configuration exists, the cytosine member of the pair can be methylated (a methyl group is added). This modification changes how the DNA interacts with proteins, including the histone proteins that control access to the region. Highly methylated (hypermethylated) DNA regions with deacetylated histones are tightly coiled and transcriptionally inactive.



Histone proteins and DNA nucleotides can be modified

chemically. Modifications affect nucleosome spacing and gene expression. (credit: modification of work by NIH)

This type of gene regulation is called epigenetic regulation. Epigenetic means “around genetics.” The changes that occur to the histone proteins and DNA do not alter the nucleotide sequence and are not permanent. Instead, these changes are temporary (although they often persist through multiple rounds of cell division) and alter the chromosomal structure (open or closed) as needed. A gene can be turned on or off depending upon the location and modifications to the histone proteins and DNA. If a gene is to be transcribed, the histone proteins and DNA are modified surrounding the chromosomal region encoding that gene. This opens the chromosomal region to allow access for RNA polymerase and other proteins, called **transcription factors**, to bind to the promoter region, located just upstream of the gene, and initiate transcription. If a gene is to remain turned off, or silenced, the histone proteins and DNA have different modifications that signal a closed chromosomal configuration. In this closed configuration, the RNA polymerase and transcription factors do not have access to the DNA and transcription cannot occur ([link](#)).

Note:

Link to Learning



View [this video](#) that describes how epigenetic regulation controls gene expression.

Section Summary

In eukaryotic cells, the first stage of gene expression control occurs at the epigenetic level. Epigenetic mechanisms control access to the chromosomal region to allow genes to be turned on or off. These mechanisms control how DNA is packed into the nucleus by regulating how tightly the DNA is wound around histone proteins. The addition or removal of chemical modifications (or flags) to histone proteins or DNA signals to the cell to open or close a chromosomal region. Therefore, eukaryotic cells can control whether a gene is expressed by controlling accessibility to transcription factors and the binding of RNA polymerase to initiate transcription.

Art Connections

Exercise:

Problem:

[\[link\]](#) In females, one of the two X chromosomes is inactivated during embryonic development because of epigenetic changes to the chromatin. What impact do you think these changes would have on nucleosome packing?

Solution:

[\[link\]](#) The nucleosomes would pack more tightly together.

Review Questions

Exercise:

Problem: What are epigenetic modifications?

- a. the addition of reversible changes to histone proteins and DNA
- b. the removal of nucleosomes from the DNA
- c. the addition of more nucleosomes to the DNA
- d. mutation of the DNA sequence

Solution:

A

Exercise:

Problem: Which of the following are true of epigenetic changes?

- a. allow DNA to be transcribed
- b. move histones to open or close a chromosomal region
- c. are temporary
- d. all of the above

Solution:

D

Free Response

Exercise:

Problem:

In cancer cells, alteration to epigenetic modifications turns off genes that are normally expressed. Hypothetically, how could you reverse this process to turn these genes back on?

Solution:

You can create medications that reverse the epigenetic processes (to add histone acetylation marks or to remove DNA methylation) and create an open chromosomal configuration.

Glossary

transcription factor

protein that binds to the DNA at the promoter or enhancer region and that influences transcription of a gene

Bis2A 14.3 Cancer and Gene Regulation

By the end of this section, you will be able to:

- Describe how changes to gene expression can cause cancer
- Explain how changes to gene expression at different levels can disrupt the cell cycle
- Discuss how understanding regulation of gene expression can lead to better drug design

Cancer is not a single disease but includes many different diseases. In cancer cells, mutations modify cell-cycle control and cells don't stop growing as they normally would. Mutations can also alter the growth rate or the progression of the cell through the cell cycle. One example of a gene modification that alters the growth rate is increased phosphorylation of cyclin B, a protein that controls the progression of a cell through the cell cycle and serves as a cell-cycle checkpoint protein.

For cells to move through each phase of the cell cycle, the cell must pass through checkpoints. This ensures that the cell has properly completed the step and has not encountered any mutation that will alter its function. Many proteins, including cyclin B, control these checkpoints. The phosphorylation of cyclin B, a post-translational event, alters its function. As a result, cells can progress through the cell cycle unimpeded, even if mutations exist in the cell and its growth should be terminated. This post-translational change of cyclin B prevents it from controlling the cell cycle and contributes to the development of cancer.

Cancer: Disease of Altered Gene Expression

Cancer can be described as a disease of altered gene expression. There are many proteins that are turned on or off (gene activation or gene silencing) that dramatically alter the overall activity of the cell. A gene that is not normally expressed in that cell can be switched on and expressed at high levels. This can be the result of gene mutation or changes in gene regulation (epigenetic, transcription, post-transcription, translation, or post-translation).

Changes in epigenetic regulation, transcription, RNA stability, protein translation, and post-translational control can be detected in cancer. While these changes don't occur simultaneously in one cancer, changes at each of these levels can be detected when observing cancer at different sites in different individuals. Therefore, changes in **histone acetylation** (epigenetic modification that leads to gene silencing), activation of transcription factors by phosphorylation, increased RNA stability, increased translational control, and protein modification can all be detected at some point in various cancer cells. Scientists are working to understand the common changes that give rise to certain types of cancer or how a modification might be exploited to destroy a tumor cell.

Tumor Suppressor Genes, Oncogenes, and Cancer

In normal cells, some genes function to prevent excess, inappropriate cell growth. These are tumor suppressor genes, which are active in normal cells to prevent uncontrolled cell growth. There are many tumor suppressor genes in cells. The most studied tumor suppressor gene is p53, which is mutated in over 50 percent of all cancer types. The p53 protein itself functions as a transcription factor. It can bind to sites in the promoters of genes to initiate transcription. Therefore, the mutation of p53 in cancer will dramatically alter the transcriptional activity of its target genes.

Note:

Link to Learning



Watch [this animation](#) to learn more about the use of p53 in fighting cancer.

Proto-oncogenes are positive cell-cycle regulators. When mutated, proto-oncogenes can become oncogenes and cause cancer. Overexpression of the oncogene can lead to uncontrolled cell growth. This is because oncogenes can alter transcriptional activity, stability, or protein translation of another gene that directly or indirectly controls cell growth. An example of an oncogene involved in cancer is a protein called myc. **Myc** is a transcription factor that is aberrantly activated in Burkett's Lymphoma, a cancer of the lymph system. Overexpression of myc transforms normal B cells into cancerous cells that continue to grow uncontrollably. High B-cell numbers can result in tumors that can interfere with normal bodily function. Patients with Burkett's lymphoma can develop tumors on their jaw or in their mouth that interfere with the ability to eat.

Cancer and Epigenetic Alterations

Silencing genes through epigenetic mechanisms is also very common in cancer cells. There are characteristic modifications to histone proteins and DNA that are associated with silenced genes. In cancer cells, the DNA in the promoter region of silenced genes is methylated on cytosine DNA residues in CpG islands. Histone proteins that surround that region lack the acetylation modification that is present when the genes are expressed in normal cells. This combination of DNA methylation and histone deacetylation (epigenetic modifications that lead to gene silencing) is commonly found in cancer. When these modifications occur, the gene present in that chromosomal region is silenced. Increasingly, scientists understand how epigenetic changes are altered in cancer. Because these changes are temporary and can be reversed—for example, by preventing the action of the histone deacetylase protein that removes acetyl groups, or by DNA methyl transferase enzymes that add methyl groups to cytosines in DNA—it is possible to design new drugs and new therapies to take advantage of the reversible nature of these processes. Indeed, many researchers are testing how a silenced gene can be switched back on in a cancer cell to help re-establish normal growth patterns.

Genes involved in the development of many other illnesses, ranging from allergies to inflammation to autism, are thought to be regulated by

epigenetic mechanisms. As our knowledge of how genes are controlled deepens, new ways to treat diseases like cancer will emerge.

Cancer and Transcriptional Control

Alterations in cells that give rise to cancer can affect the transcriptional control of gene expression. Mutations that activate transcription factors, such as increased phosphorylation, can increase the binding of a transcription factor to its binding site in a promoter. This could lead to increased transcriptional activation of that gene that results in modified cell growth. Alternatively, a mutation in the DNA of a promoter or enhancer region can increase the binding ability of a transcription factor. This could also lead to the increased transcription and aberrant gene expression that is seen in cancer cells.

Researchers have been investigating how to control the transcriptional activation of gene expression in cancer. Identifying how a transcription factor binds, or a pathway that activates where a gene can be turned off, has led to new drugs and new ways to treat cancer. In breast cancer, for example, many proteins are overexpressed. This can lead to increased phosphorylation of key transcription factors that increase transcription. One such example is the overexpression of the epidermal growth factor receptor (EGFR) in a subset of breast cancers. The EGFR pathway activates many protein kinases that, in turn, activate many transcription factors that control genes involved in cell growth. New drugs that prevent the activation of EGFR have been developed and are used to treat these cancers.

Cancer and Post-transcriptional Control

Changes in the post-transcriptional control of a gene can also result in cancer. Recently, several groups of researchers have shown that specific cancers have altered expression of miRNAs. Because miRNAs bind to the 3' UTR of RNA molecules to degrade them, overexpression of these miRNAs could be detrimental to normal cellular activity. Too many miRNAs could dramatically decrease the RNA population leading to a decrease in protein expression. Several studies have demonstrated a change in the miRNA population in specific cancer types. It appears that the subset

of miRNAs expressed in breast cancer cells is quite different from the subset expressed in lung cancer cells or even from normal breast cells. This suggests that alterations in miRNA activity can contribute to the growth of breast cancer cells. These types of studies also suggest that if some miRNAs are specifically expressed only in cancer cells, they could be potential drug targets. It would, therefore, be conceivable that new drugs that turn off miRNA expression in cancer could be an effective method to treat cancer.

Cancer and Translational/Post-translational Control

There are many examples of how translational or post-translational modifications of proteins arise in cancer. Modifications are found in cancer cells from the increased translation of a protein to changes in protein phosphorylation to alternative splice variants of a protein. An example of how the expression of an alternative form of a protein can have dramatically different outcomes is seen in colon cancer cells. The c-Flip protein, a protein involved in mediating the cell death pathway, comes in two forms: long (c-FLIPL) and short (c-FLIPS). Both forms appear to be involved in initiating controlled cell death mechanisms in normal cells. However, in colon cancer cells, expression of the long form results in increased cell growth instead of cell death. Clearly, the expression of the wrong protein dramatically alters cell function and contributes to the development of cancer.

New Drugs to Combat Cancer: Targeted Therapies

Scientists are using what is known about the regulation of gene expression in disease states, including cancer, to develop new ways to treat and prevent disease development. Many scientists are designing drugs on the basis of the gene expression patterns within individual tumors. This idea, that therapy and medicines can be tailored to an individual, has given rise to the field of personalized medicine. With an increased understanding of gene regulation and gene function, medicines can be designed to specifically target diseased cells without harming healthy cells. Some new medicines, called targeted therapies, have exploited the overexpression of a specific

protein or the mutation of a gene to develop a new medication to treat disease. One such example is the use of anti-EGF receptor medications to treat the subset of breast cancer tumors that have very high levels of the EGF protein. Undoubtedly, more targeted therapies will be developed as scientists learn more about how gene expression changes can cause cancer.

Note:

Career Connection

Clinical Trial Coordinator

A clinical trial coordinator is the person managing the proceedings of the clinical trial. This job includes coordinating patient schedules and appointments, maintaining detailed notes, building the database to track patients (especially for long-term follow-up studies), ensuring proper documentation has been acquired and accepted, and working with the nurses and doctors to facilitate the trial and publication of the results. A clinical trial coordinator may have a science background, like a nursing degree, or other certification. People who have worked in science labs or in clinical offices are also qualified to become a clinical trial coordinator. These jobs are generally in hospitals; however, some clinics and doctor's offices also conduct clinical trials and may hire a coordinator.

Section Summary

Cancer can be described as a disease of altered gene expression. Changes at every level of eukaryotic gene expression can be detected in some form of cancer at some point in time. In order to understand how changes to gene expression can cause cancer, it is critical to understand how each stage of gene regulation works in normal cells. By understanding the mechanisms of control in normal, non-diseased cells, it will be easier for scientists to understand what goes wrong in disease states including complex ones like cancer.

Review Questions

Exercise:

Problem: Cancer causing genes are called _____.

- a. transformation genes
- b. tumor suppressor genes
- c. oncogenes
- d. mutated genes

Solution:

C

Exercise:**Problem:**

Targeted therapies are used in patients with a set gene expression pattern. A targeted therapy that prevents the activation of the estrogen receptor in breast cancer would be beneficial to which type of patient?

- a. patients who express the EGFR receptor in normal cells
- b. patients with a mutation that inactivates the estrogen receptor
- c. patients with lots of the estrogen receptor expressed in their tumor
- d. patients that have no estrogen receptor expressed in their tumor

Solution:

C

Free Response**Exercise:**

Problem:

New drugs are being developed that decrease DNA methylation and prevent the removal of acetyl groups from histone proteins. Explain how these drugs could affect gene expression to help kill tumor cells.

Solution:

These drugs will keep the histone proteins and the DNA methylation patterns in the open chromosomal configuration so that transcription is feasible. If a gene is silenced, these drugs could reverse the epigenetic configuration to re-express the gene.

Exercise:**Problem:**

How can understanding the gene expression pattern in a cancer cell tell you something about that specific form of cancer?

Solution:

Understanding which genes are expressed in a cancer cell can help diagnose the specific form of cancer. It can also help identify treatment options for that patient. For example, if a breast cancer tumor expresses the EGFR in high numbers, it might respond to specific anti-EGFR therapy. If that receptor is not expressed, it would not respond to that therapy.

Glossary

DNA methylation

epigenetic modification that leads to gene silencing; commonly found in cancer cells

histone acetylation

epigenetic modification that leads to gene silencing; commonly found in cancer cells found in cancer cells

myc

oncogene that causes cancer in many cancer cells

Bis2A 14.4 Genomics and Proteomics

By the end of this section, you will be able to:

- Define genomics and proteomics
- Define whole genome sequencing
- Explain different applications of genomics and proteomics

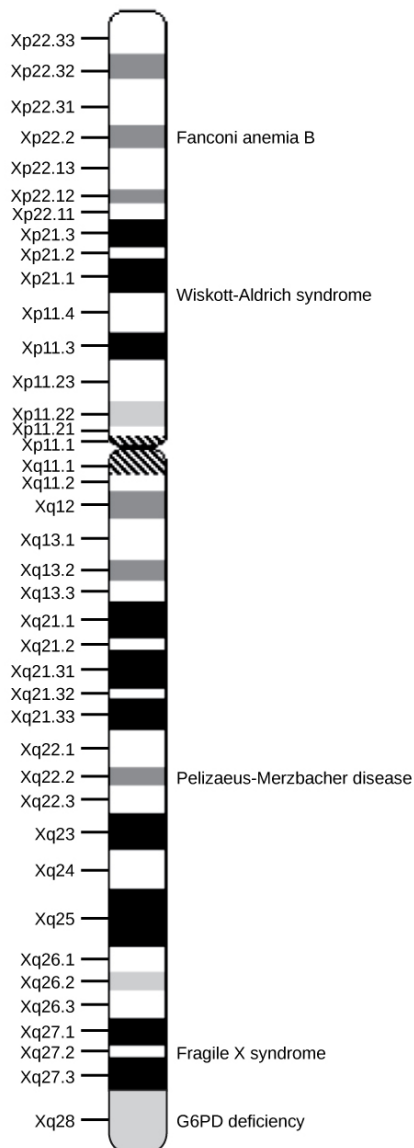
The study of nucleic acids began with the discovery of DNA, progressed to the study of genes and small fragments, and has now exploded to the field of **genomics**. Genomics is the study of entire genomes, including the complete set of genes, their nucleotide sequence and organization, and their interactions within a species and with other species. The advances in genomics have been made possible by DNA sequencing technology. Just as information technology has led to Google Maps that enable us to get detailed information about locations around the globe, genomic information is used to create similar maps of the DNA of different organisms.

Mapping Genomes

Genome mapping is the process of finding the location of genes on each chromosome. The maps that are created are comparable to the maps that we use to navigate streets. A **genetic map** is an illustration that lists genes and their location on a chromosome. Genetic maps provide the big picture (similar to a map of interstate highways) and use genetic markers (similar to landmarks). A genetic marker is a gene or sequence on a chromosome that shows genetic linkage with a trait of interest. The genetic marker tends to be inherited with the gene of interest, and one measure of distance between them is the recombination frequency during meiosis. Early geneticists called this linkage analysis.

Physical maps get into the intimate details of smaller regions of the chromosomes (similar to a detailed road map) ([link](#)). A physical map is a representation of the physical distance, in nucleotides, between genes or genetic markers. Both genetic linkage maps and physical maps are required to build a complete picture of the genome. Having a complete map of the genome makes it easier for researchers to study individual genes. Human genome maps help researchers in their efforts to identify human disease-

causing genes related to illnesses such as cancer, heart disease, and cystic fibrosis, to name a few. In addition, genome mapping can be used to help identify organisms with beneficial traits, such as microbes with the ability to clean up pollutants or even prevent pollution. Research involving plant genome mapping may lead to methods that produce higher crop yields or to the development of plants that adapt better to climate change.



This is a physical map of
the human X

chromosome. (credit:
modification of work by
NCBI, NIH)

Genetic maps provide the outline, and physical maps provide the details. It is easy to understand why both types of genome-mapping techniques are important to show the big picture. Information obtained from each technique is used in combination to study the genome. Genomic mapping is used with different model organisms that are used for research. Genome mapping is still an ongoing process, and as more advanced techniques are developed, more advances are expected. Genome mapping is similar to completing a complicated puzzle using every piece of available data. Mapping information generated in laboratories all over the world is entered into central databases, such as the National Center for Biotechnology Information (NCBI). Efforts are made to make the information more easily accessible to researchers and the general public. Just as we use global positioning systems instead of paper maps to navigate through roadways, NCBI allows us to use a genome viewer tool to simplify the data mining process.

Note:

Concept in Action



[Online Mendelian Inheritance in Man \(OMIM\)](#) is a searchable online catalog of human genes and genetic disorders. This website shows genome mapping, and also details the history and research of each trait and

disorder. Click the link to search for traits (such as handedness) and genetic disorders (such as diabetes).

Whole Genome Sequencing

Although there have been significant advances in the medical sciences in recent years, doctors are still confounded by many diseases and researchers are using whole genome sequencing to get to the bottom of the problem.

Whole genome sequencing is a process that determines the DNA sequence of an entire genome. Whole genome sequencing is a brute-force approach to problem solving when there is a genetic basis at the core of a disease. Several laboratories now provide services to sequence, analyze, and interpret entire genomes.

In 2010, whole genome sequencing was used to save a young boy whose intestines had multiple mysterious abscesses. The child had several colon operations with no relief. Finally, a whole genome sequence revealed a defect in a pathway that controls apoptosis (programmed cell death). A bone marrow transplant was used to overcome this genetic disorder, leading to a cure for the boy. He was the first person to be successfully diagnosed using whole genome sequencing.

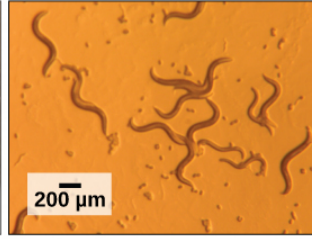
The first genomes to be sequenced, such as those belonging to viruses, bacteria, and yeast, were smaller in terms of the number of nucleotides than the genomes of multicellular organisms. The genomes of other model organisms, such as the mouse (*Mus musculus*), the fruit fly (*Drosophila melanogaster*), and the nematode (*Caenorhabditis elegans*) are now known. A great deal of basic research is performed in **model organisms** because the information can be applied to other organisms. A model organism is a species that is studied as a model to understand the biological processes in other species that can be represented by the model organism. For example, fruit flies are able to metabolize alcohol like humans, so the genes affecting sensitivity to alcohol have been studied in fruit flies in an effort to understand the variation in sensitivity to alcohol in humans. Having entire genomes sequenced helps with the research efforts in these model organisms ([link](#)).



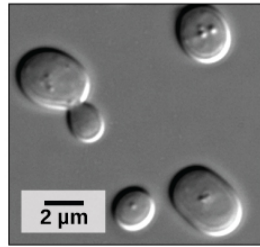
Mus musculus



Drosophila melanogaster



Caenorhabditis elegans



Saccharomyces cerevisiae



Arabidopsis thaliana

Much basic research is done with model organisms, such as the mouse, *Mus musculus*; the fruit fly, *Drosophila melanogaster*; the nematode *Caenorhabditis elegans*; the yeast *Saccharomyces cerevisiae*; and the common weed, *Arabidopsis thaliana*. (credit "mouse": modification of work by Florean Fortescue; credit "nematodes": modification of work by "snickclunk"/Flickr; credit "common weed": modification of work by Peggy Greb, USDA; scale-bar data from Matt Russell)

The first human genome sequence was published in 2003. The number of whole genomes that have been sequenced steadily increases and now includes hundreds of species and thousands of individual human genomes.

Applying Genomics

The introduction of DNA sequencing and whole genome sequencing projects, particularly the Human Genome Project, has expanded the applicability of DNA sequence information. Genomics is now being used in

a wide variety of fields, such as metagenomics, pharmacogenomics, and mitochondrial genomics. The most commonly known application of genomics is to understand and find cures for diseases.

Predicting Disease Risk at the Individual Level

Predicting the risk of disease involves screening and identifying currently healthy individuals by genome analysis at the individual level. Intervention with lifestyle changes and drugs can be recommended before disease onset. However, this approach is most applicable when the problem arises from a single gene mutation. Such defects only account for about 5 percent of diseases found in developed countries. Most of the common diseases, such as heart disease, are multifactorial or polygenic, which refers to a phenotypic characteristic that is determined by two or more genes, and also environmental factors such as diet. In April 2010, scientists at Stanford University published the genome analysis of a healthy individual (Stephen Quake, a scientist at Stanford University, who had his genome sequenced); the analysis predicted his propensity to acquire various diseases. A risk assessment was done to analyze Quake's percentage of risk for 55 different medical conditions. A rare genetic mutation was found that showed him to be at risk for sudden heart attack. He was also predicted to have a 23 percent risk of developing prostate cancer and a 1.4 percent risk of developing Alzheimer's disease. The scientists used databases and several publications to analyze the genomic data. Even though genomic sequencing is becoming more affordable and analytical tools are becoming more reliable, ethical issues surrounding genomic analysis at a population level remain to be addressed. For example, could such data be legitimately used to charge more or less for insurance or to affect credit ratings?

Genome-wide Association Studies

Since 2005, it has been possible to conduct a type of study called a genome-wide association study, or GWAS. A GWAS is a method that identifies differences between individuals in single nucleotide polymorphisms (SNPs)

that may be involved in causing diseases. The method is particularly suited to diseases that may be affected by one or many genetic changes throughout the genome. It is very difficult to identify the genes involved in such a disease using family history information. The GWAS method relies on a genetic database that has been in development since 2002 called the International HapMap Project. The HapMap Project sequenced the genomes of several hundred individuals from around the world and identified groups of SNPs. The groups include SNPs that are located near to each other on chromosomes so they tend to stay together through recombination. The fact that the group stays together means that identifying one marker SNP is all that is needed to identify all the SNPs in the group. There are several million SNPs identified, but identifying them in other individuals who have not had their complete genome sequenced is much easier because only the marker SNPs need to be identified.

In a common design for a GWAS, two groups of individuals are chosen; one group has the disease, and the other group does not. The individuals in each group are matched in other characteristics to reduce the effect of confounding variables causing differences between the two groups. For example, the genotypes may differ because the two groups are mostly taken from different parts of the world. Once the individuals are chosen, and typically their numbers are a thousand or more for the study to work, samples of their DNA are obtained. The DNA is analyzed using automated systems to identify large differences in the percentage of particular SNPs between the two groups. Often the study examines a million or more SNPs in the DNA. The results of GWAS can be used in two ways: the genetic differences may be used as markers for susceptibility to the disease in undiagnosed individuals, and the particular genes identified can be targets for research into the molecular pathway of the disease and potential therapies. An offshoot of the discovery of gene associations with disease has been the formation of companies that provide so-called “personal genomics” that will identify risk levels for various diseases based on an individual’s SNP complement. The science behind these services is controversial.

Because GWAS looks for associations between genes and disease, these studies provide data for other research into causes, rather than answering

specific questions themselves. An association between a gene difference and a disease does not necessarily mean there is a cause-and-effect relationship. However, some studies have provided useful information about the genetic causes of diseases. For example, three different studies in 2005 identified a gene for a protein involved in regulating inflammation in the body that is associated with a disease-causing blindness called age-related macular degeneration. This opened up new possibilities for research into the cause of this disease. A large number of genes have been identified to be associated with Crohn's disease using GWAS, and some of these have suggested new hypothetical mechanisms for the cause of the disease.

Pharmacogenomics

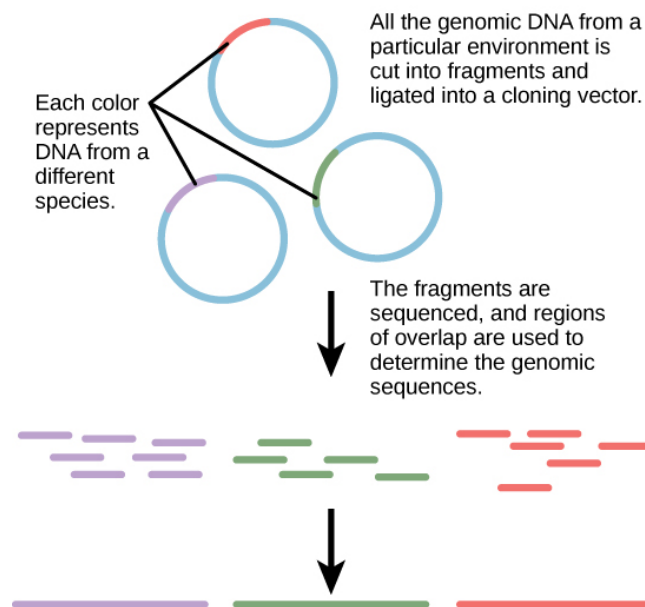
Pharmacogenomics involves evaluating the effectiveness and safety of drugs on the basis of information from an individual's genomic sequence. Personal genome sequence information can be used to prescribe medications that will be most effective and least toxic on the basis of the individual patient's genotype. Studying changes in gene expression could provide information about the gene transcription profile in the presence of the drug, which can be used as an early indicator of the potential for toxic effects. For example, genes involved in cellular growth and controlled cell death, when disturbed, could lead to the growth of cancerous cells. Genome-wide studies can also help to find new genes involved in drug toxicity. The gene signatures may not be completely accurate, but can be tested further before pathologic symptoms arise.

Metagenomics

Traditionally, microbiology has been taught with the view that microorganisms are best studied under pure culture conditions, which involves isolating a single type of cell and culturing it in the laboratory. Because microorganisms can go through several generations in a matter of hours, their gene expression profiles adapt to the new laboratory environment very quickly. On the other hand, many species resist being

cultured in isolation. Most microorganisms do not live as isolated entities, but in microbial communities known as biofilms. For all of these reasons, pure culture is not always the best way to study microorganisms.

Metagenomics is the study of the collective genomes of multiple species that grow and interact in an environmental niche. Metagenomics can be used to identify new species more rapidly and to analyze the effect of pollutants on the environment ([\[link\]](#)). Metagenomics techniques can now also be applied to communities of higher eukaryotes, such as fish.



Metagenomics involves isolating DNA from multiple species within an environmental niche. The DNA is cut up and sequenced, allowing entire genome sequences of multiple species to be reconstructed from the sequences of overlapping pieces.

Creation of New Biofuels

Knowledge of the genomics of microorganisms is being used to find better ways to harness biofuels from algae and cyanobacteria. The primary sources of fuel today are coal, oil, wood, and other plant products such as ethanol. Although plants are renewable resources, there is still a need to find more alternative renewable sources of energy to meet our population's energy demands. The microbial world is one of the largest resources for genes that encode new enzymes and produce new organic compounds, and it remains largely untapped. This vast genetic resource holds the potential to provide new sources of biofuels ([\[link\]](#)).



Renewable fuels were tested in Navy ships and aircraft at the first Naval Energy Forum. (credit: modification of work by

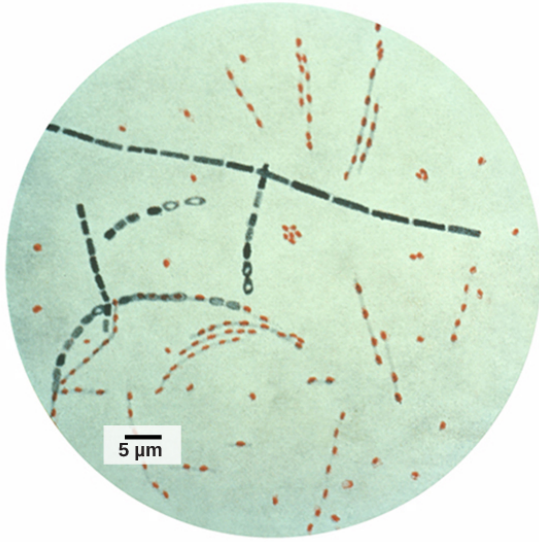
John F. Williams, US
Navy)

Mitochondrial Genomics

Mitochondria are intracellular organelles that contain their own DNA. Mitochondrial DNA mutates at a rapid rate and is often used to study evolutionary relationships. Another feature that makes studying the mitochondrial genome interesting is that in most multicellular organisms, the mitochondrial DNA is passed on from the mother during the process of fertilization. For this reason, mitochondrial genomics is often used to trace genealogy.

Genomics in Forensic Analysis

Information and clues obtained from DNA samples found at crime scenes have been used as evidence in court cases, and genetic markers have been used in forensic analysis. Genomic analysis has also become useful in this field. In 2001, the first use of genomics in forensics was published. It was a collaborative effort between academic research institutions and the FBI to solve the mysterious cases of anthrax ([\[link\]](#)) that was transported by the US Postal Service. Anthrax bacteria were made into an infectious powder and mailed to news media and two U.S. Senators. The powder infected the administrative staff and postal workers who opened or handled the letters. Five people died, and 17 were sickened from the bacteria. Using microbial genomics, researchers determined that a specific strain of anthrax was used in all the mailings; eventually, the source was traced to a scientist at a national biodefense laboratory in Maryland.



Bacillus anthracis is the organism that causes anthrax. (credit: modification of work by CDC; scale-bar data from Matt Russell)

Genomics in Agriculture

Genomics can reduce the trials and failures involved in scientific research to a certain extent, which could improve the quality and quantity of crop yields in agriculture ([link](#)). Linking traits to genes or gene signatures helps to improve crop breeding to generate hybrids with the most desirable qualities. Scientists use genomic data to identify desirable traits, and then transfer those traits to a different organism to create a new genetically modified organism, as described in the previous module. Scientists are discovering how genomics can improve the quality and quantity of agricultural production. For example, scientists could use desirable traits to create a useful product or enhance an existing product, such as making a drought-sensitive crop more tolerant of the dry season.



Transgenic agricultural plants can be made to resist disease. These transgenic plums are resistant to the plum pox virus. (credit: Scott Bauer, USDA ARS)

Proteomics

Proteins are the final products of genes that perform the function encoded by the gene. Proteins are composed of amino acids and play important roles in the cell. All enzymes (except ribozymes) are proteins and act as catalysts that affect the rate of reactions. Proteins are also regulatory molecules, and some are hormones. Transport proteins, such as hemoglobin, help transport oxygen to various organs. Antibodies that defend against foreign particles are also proteins. In the diseased state, protein function can be impaired because of changes at the genetic level or because of direct impact on a specific protein.

A proteome is the entire set of proteins produced by a cell type. Proteomes can be studied using the knowledge of genomes because genes code for mRNAs, and the mRNAs encode proteins. The study of the function of proteomes is called **proteomics**. Proteomics complements genomics and is

useful when scientists want to test their hypotheses that were based on genes. Even though all cells in a multicellular organism have the same set of genes, the set of proteins produced in different tissues is different and dependent on gene expression. Thus, the genome is constant, but the proteome varies and is dynamic within an organism. In addition, RNAs can be alternatively spliced (cut and pasted to create novel combinations and novel proteins), and many proteins are modified after translation. Although the genome provides a blueprint, the final architecture depends on several factors that can change the progression of events that generate the proteome.

Genomes and proteomes of patients suffering from specific diseases are being studied to understand the genetic basis of the disease. The most prominent disease being studied with proteomic approaches is cancer ([link](#)). Proteomic approaches are being used to improve the screening and early detection of cancer; this is achieved by identifying proteins whose expression is affected by the disease process. An individual protein is called a **biomarker**, whereas a set of proteins with altered expression levels is called a **protein signature**. For a biomarker or protein signature to be useful as a candidate for early screening and detection of a cancer, it must be secreted in body fluids such as sweat, blood, or urine, so that large-scale screenings can be performed in a noninvasive fashion. The current problem with using biomarkers for the early detection of cancer is the high rate of false-negative results. A false-negative result is a negative test result that should have been positive. In other words, many cases of cancer go undetected, which makes biomarkers unreliable. Some examples of protein biomarkers used in cancer detection are CA-125 for ovarian cancer and PSA for prostate cancer. Protein signatures may be more reliable than biomarkers to detect cancer cells. Proteomics is also being used to develop individualized treatment plans, which involves the prediction of whether or not an individual will respond to specific drugs and the side effects that the individual may have. Proteomics is also being used to predict the possibility of disease recurrence.



This machine is preparing to do a proteomic pattern analysis to identify specific cancers so that an accurate cancer prognosis can be made. (credit: Dorie Hightower, NCI, NIH)

The National Cancer Institute has developed programs to improve the detection and treatment of cancer. The Clinical Proteomic Technologies for Cancer and the Early Detection Research Network are efforts to identify protein signatures specific to different types of cancers. The Biomedical Proteomics Program is designed to identify protein signatures and design effective therapies for cancer patients.

Section Summary

Genome mapping is similar to solving a big, complicated puzzle with pieces of information coming from laboratories all over the world. Genetic maps provide an outline for the location of genes within a genome, and they estimate the distance between genes and genetic markers on the basis of the recombination frequency during meiosis. Physical maps provide detailed information about the physical distance between the genes. The most detailed information is available through sequence mapping. Information

from all mapping and sequencing sources is combined to study an entire genome.

Whole genome sequencing is the latest available resource to treat genetic diseases. Some doctors are using whole genome sequencing to save lives. Genomics has many industrial applications, including biofuel development, agriculture, pharmaceuticals, and pollution control.

Imagination is the only barrier to the applicability of genomics. Genomics is being applied to most fields of biology; it can be used for personalized medicine, prediction of disease risks at an individual level, the study of drug interactions before the conduction of clinical trials, and the study of microorganisms in the environment as opposed to the laboratory. It is also being applied to the generation of new biofuels, genealogical assessment using mitochondria, advances in forensic science, and improvements in agriculture.

Proteomics is the study of the entire set of proteins expressed by a given type of cell under certain environmental conditions. In a multicellular organism, different cell types will have different proteomes, and these will vary with changes in the environment. Unlike a genome, a proteome is dynamic and under constant flux, which makes it more complicated and more useful than the knowledge of genomes alone.

Multiple Choice

Exercise:

Problem:

What is the most challenging issue facing genome sequencing?

- a. the inability to develop fast and accurate sequencing techniques
 - b. the ethics of using information from genomes at the individual level
 - c. the availability and stability of DNA
 - d. all of the above
-

Solution:

B

Exercise:

Problem: Genomics can be used in agriculture to:

- a. generate new hybrid strains
- b. improve disease resistance
- c. improve yield
- d. all of the above

Solution:

D

Exercise:

Problem:

What kind of diseases are studied using genome-wide association studies?

- a. viral diseases
- b. single-gene inherited diseases
- c. diseases caused by multiple genes
- d. diseases caused by environmental factors

Solution:

C

Free Response

Exercise:

Problem: Describe two of the applications for genome mapping.

Solution:

Genome mapping helps researchers to study disease-causing genes in humans. It also helps to identify traits of organisms that can be used in applications such as cleaning up pollution.

Exercise:

Problem:

Identify a possible advantage and a possible disadvantage of a genetic test that would identify genes in individuals that increase their probability of having Alzheimer's disease later in life.

Solution:

The benefit of such a test is that the individual can make preparations for having the disease including taking treatments that slow the disease. The disadvantage of the test is that it might be used by insurance companies to deny coverage to the person.

Glossary

biomarker

an individual protein that is uniquely produced in a diseased state

genetic map

an outline of genes and their location on a chromosome that is based on recombination frequencies between markers

genomics

the study of entire genomes, including the complete set of genes, their nucleotide sequence and organization, and their interactions within a species and with other species

metagenomics

the study of the collective genomes of multiple species that grow and interact in an environmental niche

model organism

a species that is studied and used as a model to understand the biological processes in other species represented by the model organism

pharmacogenomics

the study of drug interactions with the genome or proteome; also called toxicogenomics

physical map

a representation of the physical distance between genes or genetic markers

protein signature

a set of over- or under-expressed proteins characteristic of cells in a particular diseased tissue

proteomics

study of the function of proteomes

whole genome sequencing

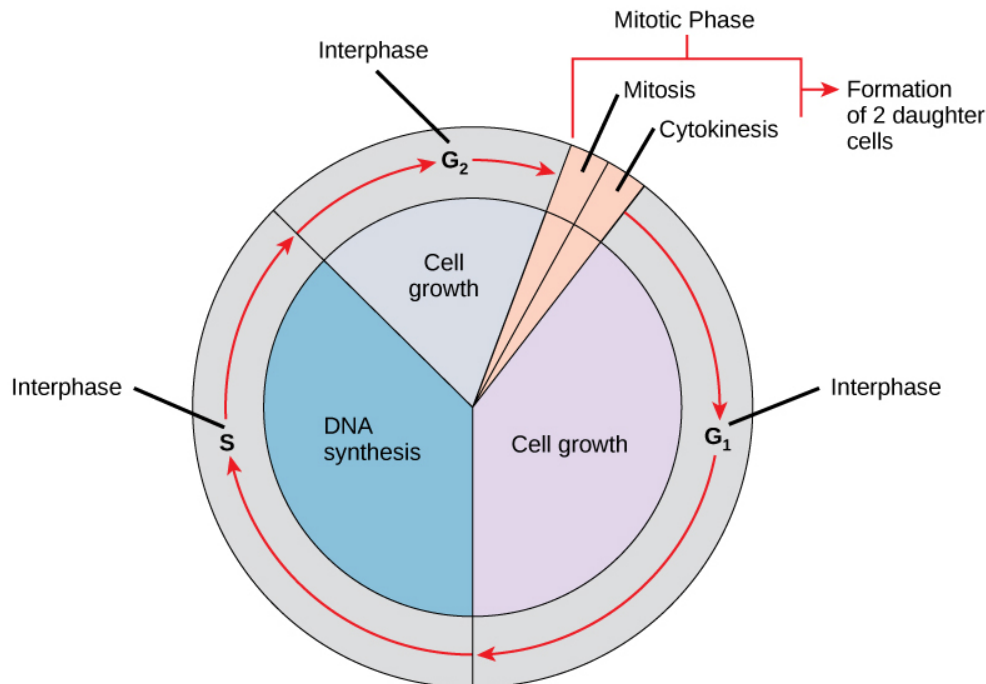
a process that determines the nucleotide sequence of an entire genome

Bis2A 15.0 The Cell Cycle

By the end of this section, you will be able to:

- Describe the three stages of interphase
- Discuss the behavior of chromosomes during mitosis and how the cytoplasmic content divides during cytokinesis
- Define the quiescent G_0 phase
- Explain how the three internal control checkpoints occur at the end of G_1 , at the G_2 –M transition, and during metaphase

The **cell cycle** is an ordered series of events involving cell growth and cell division that produces two new daughter cells. Cells on the path to cell division proceed through a series of precisely timed and carefully regulated stages of growth, DNA replication, and division that produce two genetically identical cells. The cell cycle has two major phases: interphase and the mitotic phase ([link]). During **interphase**, the cell grows and DNA is replicated. During the **mitotic phase**, the replicated DNA and cytoplasmic contents are separated and the cell divides. Watch this video about the cell cycle: <https://www.youtube.com/watch?v=Wy3N5NCZBHQ>



A cell moves through a series of phases in an orderly manner. During interphase, G_1 involves cell growth and

protein synthesis, the S phase involves DNA replication and the replication of the centrosome, and G₂ involves further growth and protein synthesis. The mitotic phase follows interphase. Mitosis is nuclear division during which duplicated chromosomes are segregated and distributed into daughter nuclei. Usually the cell will divide after mitosis in a process called cytokinesis in which the cytoplasm is divided and two daughter cells are formed.

Interphase

During interphase, the cell undergoes normal processes while also preparing for cell division. For a cell to move from interphase to the mitotic phase, many internal and external conditions must be met. The three stages of interphase are called G₁, S, and G₂.

G₁ Phase

The first stage of interphase is called the **G₁ phase**, or first gap, because little change is visible. However, during the G₁ stage, the cell is quite active at the biochemical level. The cell is accumulating the building blocks of chromosomal DNA and the associated proteins, as well as accumulating enough energy reserves to complete the task of replicating each chromosome in the nucleus.

S Phase

Throughout interphase, nuclear DNA remains in a semi-condensed chromatin configuration. In the **S phase** (synthesis phase), DNA replication results in the formation of two identical copies of each chromosome—sister chromatids—that are firmly attached at the centromere region. At this stage,

each chromosome is made of two sister chromatids and is a duplicated chromosome. The centrosome is duplicated during the S phase. The two centrosomes will give rise to the **mitotic spindle**, the apparatus that orchestrates the movement of chromosomes during mitosis. The centrosome consists of a pair of rod-like **centrioles** at right angles to each other. Centrioles help organize cell division. Centrioles are not present in the centrosomes of many eukaryotic species, such as plants and most fungi.

G₂ Phase

In the **G₂ phase**, or second gap, the cell replenishes its energy stores and synthesizes the proteins necessary for chromosome manipulation. Some cell organelles are duplicated, and the cytoskeleton is dismantled to provide resources for the mitotic spindle. There may be additional cell growth during G₂. The final preparations for the mitotic phase must be completed before the cell is able to enter the first stage of mitosis.

The Mitotic Phase

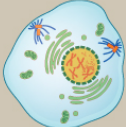
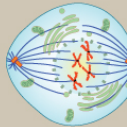
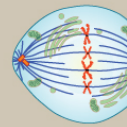
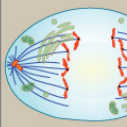
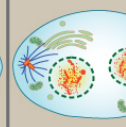
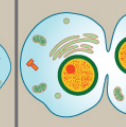
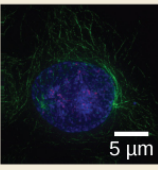
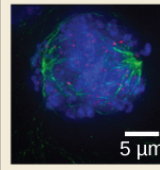
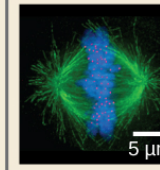
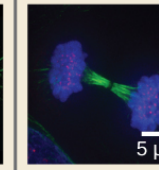
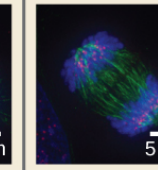
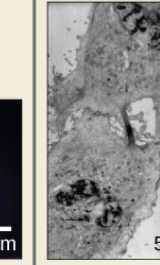
To make two daughter cells, the contents of the nucleus and the cytoplasm must be divided. The mitotic phase is a multistep process during which the duplicated chromosomes are aligned, separated, and moved to opposite poles of the cell, and then the cell is divided into two new identical daughter cells. The first portion of the mitotic phase, **mitosis**, is composed of five stages, which accomplish nuclear division. The second portion of the mitotic phase, called cytokinesis, is the physical separation of the cytoplasmic components into two daughter cells.

Mitosis

Mitosis is divided into a series of phases—prophase, prometaphase, metaphase, anaphase, and telophase—that result in the division of the cell nucleus ([\[link\]](#)).

Note:

Art Connection

Prophase	Prometaphase	Metaphase	Anaphase	Telophase	Cytokinesis
					
<ul style="list-style-type: none"> Chromosomes condense and become visible Spindle fibers emerge from the centrosomes Nuclear envelope breaks down Nucleolus disappears 	<ul style="list-style-type: none"> Chromosomes continue to condense Kinetochores appear at the centromeres Mitotic spindle microtubules attach to kinetochores Centrosomes move toward opposite poles 	<ul style="list-style-type: none"> Mitotic spindle is fully developed, centrosomes are at opposite poles of the cell Chromosomes are lined up at the metaphase plate Each sister chromatid is attached to a spindle fiber originating from opposite poles 	<ul style="list-style-type: none"> Cohesin proteins binding the sister chromatids together break down Sister chromatids (now called chromosomes) are pulled toward opposite poles Non-kinetochore spindle fibers lengthen, elongating the cell 	<ul style="list-style-type: none"> Chromosomes arrive at opposite poles and begin to decondense Nuclear envelope material surrounds each set of chromosomes The mitotic spindle breaks down 	<ul style="list-style-type: none"> Animal cells: a cleavage furrow separates the daughter cells Plant cells: a cell plate separates the daughter cells
					

MITOSIS

Animal cell mitosis is divided into five stages—prophase, prometaphase, metaphase, anaphase, and telophase—visualized here by light microscopy with fluorescence. Mitosis is usually accompanied by cytokinesis, shown here by a transmission electron microscope. (credit "diagrams": modification of work by Mariana Ruiz Villareal; credit "mitosis micrographs": modification of work by Roy van Heesbeen; credit "cytokinesis micrograph": modification of work by the Wadsworth Center, NY State Department of Health; donated to the Wikimedia foundation; scale-bar data from Matt Russell)

Which of the following is the correct order of events in mitosis?

- a. Sister chromatids line up at the metaphase plate. The kinetochore becomes attached to the mitotic spindle. The nucleus re-forms and the cell divides. The sister chromatids separate.
- b. The kinetochore becomes attached to the mitotic spindle. The sister chromatids separate. Sister chromatids line up at the metaphase plate. The nucleus re-forms and the cell divides.
- c. The kinetochore becomes attached to metaphase plate. Sister chromatids line up at the metaphase plate. The kinetochore breaks down and the sister chromatids separate. The nucleus re-forms and the cell divides.
- d. The kinetochore becomes attached to the mitotic spindle. Sister chromatids line up at the metaphase plate. The kinetochore breaks apart and the sister chromatids separate. The nucleus re-forms and the cell divides.

During **prophase**, the “first phase,” several events must occur to provide access to the chromosomes in the nucleus. The nuclear envelope starts to break into small vesicles, and the Golgi apparatus and endoplasmic reticulum fragment and disperse to the periphery of the cell. The nucleolus disappears. The centrosomes begin to move to opposite poles of the cell. The microtubules that form the basis of the mitotic spindle extend between the centrosomes, pushing them farther apart as the microtubule fibers lengthen. The sister chromatids begin to coil more tightly and become visible under a light microscope.

During **prometaphase**, many processes that were begun in prophase continue to advance and culminate in the formation of a connection between the chromosomes and cytoskeleton. The remnants of the nuclear envelope disappear. The mitotic spindle continues to develop as more microtubules assemble and stretch across the length of the former nuclear area. Chromosomes become more condensed and visually discrete. Each sister chromatid attaches to spindle microtubules at the centromere via a protein complex called the **kinetochore**.

During **metaphase**, all of the chromosomes are aligned in a plane called the **metaphase plate**, or the equatorial plane, midway between the two poles of the cell. The sister chromatids are still tightly attached to each other. At this time, the chromosomes are maximally condensed.

During **anaphase**, the sister chromatids at the equatorial plane are split apart at the centromere. Each chromatid, now called a chromosome, is pulled rapidly toward the centrosome to which its microtubule was attached. The cell becomes visibly elongated as the non-kinetochore microtubules slide against each other at the metaphase plate where they overlap.

During **telophase**, all of the events that set up the duplicated chromosomes for mitosis during the first three phases are reversed. The chromosomes reach the opposite poles and begin to decondense (unravel). The mitotic spindles are broken down into monomers that will be used to assemble cytoskeleton components for each daughter cell. Nuclear envelopes form around chromosomes.

Note:

Concept in Action



[This page of movies](#) illustrates different aspects of mitosis. Watch the movie entitled “DIC microscopy of cell division in a newt lung cell” and identify the phases of mitosis.

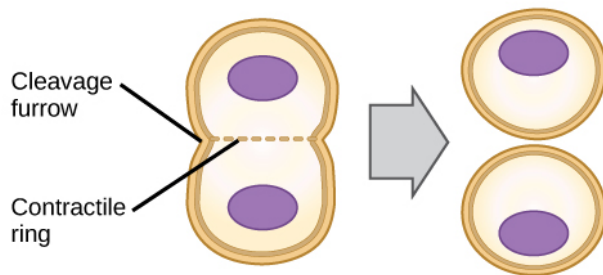
Cytokinesis

Cytokinesis is the second part of the mitotic phase during which cell division is completed by the physical separation of the cytoplasmic components into two daughter cells. Although the stages of mitosis are similar for most eukaryotes, the process of cytokinesis is quite different for eukaryotes that have cell walls, such as plant cells.

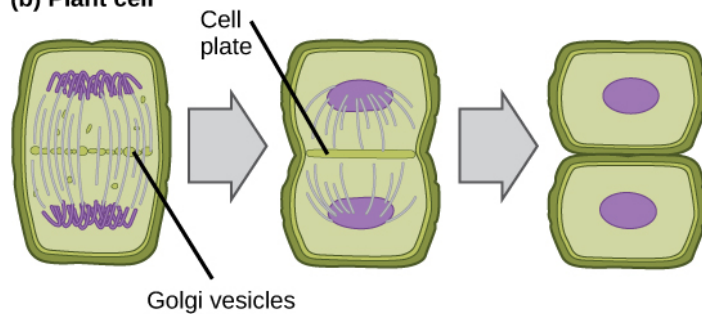
In cells such as animal cells that lack cell walls, cytokinesis begins following the onset of anaphase. A contractile ring composed of actin filaments forms just inside the plasma membrane at the former metaphase plate. The actin filaments pull the equator of the cell inward, forming a fissure. This fissure, or “crack,” is called the **cleavage furrow**. The furrow deepens as the actin ring contracts, and eventually the membrane and cell are cleaved in two ([\[link\]](#)).

In plant cells, a cleavage furrow is not possible because of the rigid cell walls surrounding the plasma membrane. A new cell wall must form between the daughter cells. During interphase, the Golgi apparatus accumulates enzymes, structural proteins, and glucose molecules prior to breaking up into vesicles and dispersing throughout the dividing cell. During telophase, these Golgi vesicles move on microtubules to collect at the metaphase plate. There, the vesicles fuse from the center toward the cell walls; this structure is called a **cell plate**. As more vesicles fuse, the cell plate enlarges until it merges with the cell wall at the periphery of the cell. Enzymes use the glucose that has accumulated between the membrane layers to build a new cell wall of cellulose. The Golgi membranes become the plasma membrane on either side of the new cell wall ([\[link\]](#)).

(a) Animal cell



(b) Plant cell

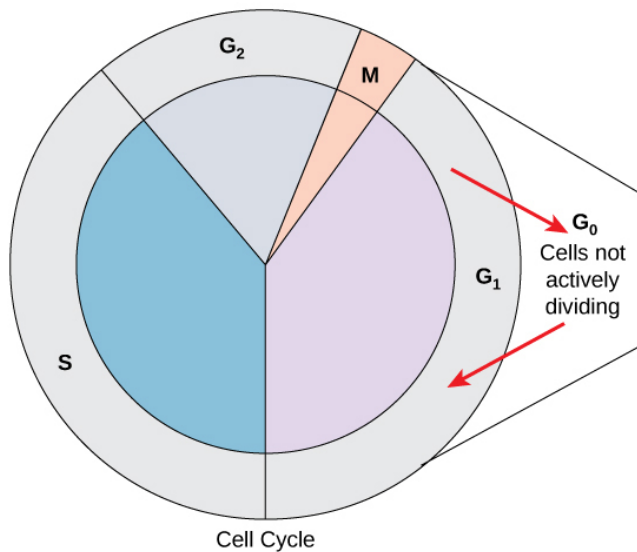


In part (a), a cleavage furrow forms at the former metaphase plate in the animal cell. The plasma membrane is drawn in by a ring of actin fibers contracting just inside the membrane. The cleavage furrow deepens until the cells are pinched in two. In part (b), Golgi vesicles coalesce at the former metaphase plate in a plant cell. The vesicles fuse and form the cell plate. The cell plate grows from the center toward the cell walls. New cell walls are made from the vesicle contents.

G₀ Phase

Not all cells adhere to the classic cell-cycle pattern in which a newly formed daughter cell immediately enters interphase, closely followed by the

mitotic phase. Cells in the **G₀ phase** are not actively preparing to divide. The cell is in a quiescent (inactive) stage, having exited the cell cycle. Some cells enter G₀ temporarily until an external signal triggers the onset of G₁. Other cells that never or rarely divide, such as mature cardiac muscle and nerve cells, remain in G₀ permanently ([\[link\]](#)).



Cells that are not actively preparing to divide enter an alternate phase called G₀. In some cases, this is a temporary condition until triggered to enter G₁. In other cases, the cell will remain in G₀ permanently.

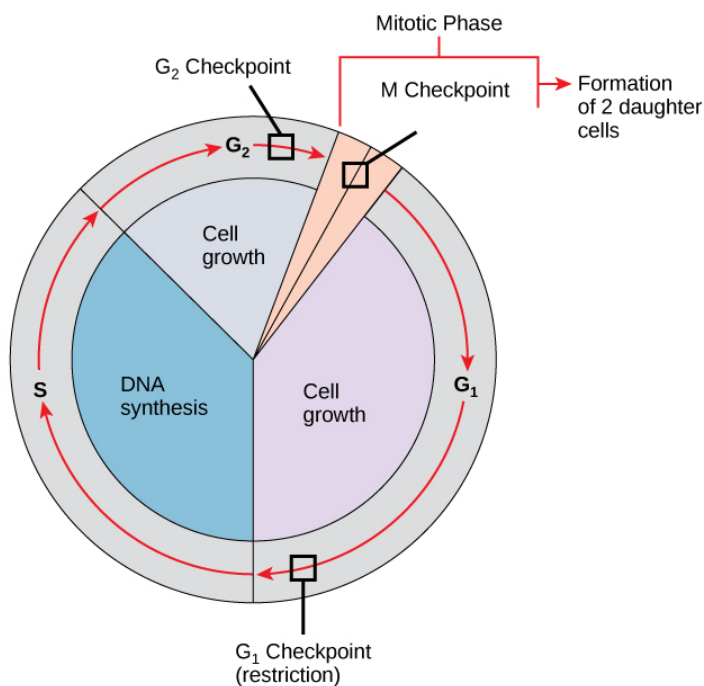
Control of the Cell Cycle

The length of the cell cycle is highly variable even within the cells of an individual organism. In humans, the frequency of cell turnover ranges from a few hours in early embryonic development to an average of two to five

days for epithelial cells, or to an entire human lifetime spent in G_0 by specialized cells such as cortical neurons or cardiac muscle cells. There is also variation in the time that a cell spends in each phase of the cell cycle. When fast-dividing mammalian cells are grown in culture (outside the body under optimal growing conditions), the length of the cycle is approximately 24 hours. In rapidly dividing human cells with a 24-hour cell cycle, the G_1 phase lasts approximately 11 hours. The timing of events in the cell cycle is controlled by mechanisms that are both internal and external to the cell.

Regulation at Internal Checkpoints

It is essential that daughter cells be exact duplicates of the parent cell. Mistakes in the duplication or distribution of the chromosomes lead to mutations that may be passed forward to every new cell produced from the abnormal cell. To prevent a compromised cell from continuing to divide, there are internal control mechanisms that operate at three main **cell cycle checkpoints** at which the cell cycle can be stopped until conditions are favorable. These checkpoints occur near the end of G_1 , at the G_2 –M transition, and during metaphase ([\[link\]](#)).



The cell cycle is controlled at three checkpoints.

Integrity of the DNA is assessed at the G_1 checkpoint. Proper chromosome duplication is assessed at the G_2 checkpoint. Attachment of each kinetochore to a spindle fiber is assessed at the M checkpoint.

The G_1 Checkpoint

The G_1 checkpoint determines whether all conditions are favorable for cell division to proceed. The G_1 checkpoint, also called the restriction point, is the point at which the cell irreversibly commits to the cell-division process. In addition to adequate reserves and cell size, there is a check for damage to the genomic DNA at the G_1 checkpoint. A cell that does not meet all the requirements will not be released into the S phase.

The G_2 Checkpoint

The G_2 checkpoint bars the entry to the mitotic phase if certain conditions are not met. As in the G_1 checkpoint, cell size and protein reserves are assessed. However, the most important role of the G_2 checkpoint is to ensure that all of the chromosomes have been replicated and that the replicated DNA is not damaged.

The M Checkpoint

The M checkpoint occurs near the end of the metaphase stage of mitosis. The M checkpoint is also known as the spindle checkpoint because it determines if all the sister chromatids are correctly attached to the spindle microtubules. Because the separation of the sister chromatids during

anaphase is an irreversible step, the cycle will not proceed until the kinetochores of each pair of sister chromatids are firmly anchored to spindle fibers arising from opposite poles of the cell.

Note:**Concept in Action**

Watch what occurs at the G_1 , G_2 , and M checkpoints by visiting [this animation](#) of the cell cycle.

Section Summary

The cell cycle is an orderly sequence of events. Cells on the path to cell division proceed through a series of precisely timed and carefully regulated stages. In eukaryotes, the cell cycle consists of a long preparatory period, called interphase. Interphase is divided into G_1 , S, and G_2 phases. Mitosis consists of five stages: prophase, prometaphase, metaphase, anaphase, and telophase. Mitosis is usually accompanied by cytokinesis, during which the cytoplasmic components of the daughter cells are separated either by an actin ring (animal cells) or by cell plate formation (plant cells).

Each step of the cell cycle is monitored by internal controls called checkpoints. There are three major checkpoints in the cell cycle: one near the end of G_1 , a second at the G_2 –M transition, and the third during metaphase.

Art Connections

Exercise:**Problem:**

[\[link\]](#) Which of the following is the correct order of events in mitosis?

- a. Sister chromatids line up at the metaphase plate. The kinetochore becomes attached to the mitotic spindle. The nucleus re-forms and the cell divides. The sister chromatids separate.
- b. The kinetochore becomes attached to the mitotic spindle. The sister chromatids separate. Sister chromatids line up at the metaphase plate. The nucleus re-forms and the cell divides.
- c. The kinetochore becomes attached to metaphase plate. Sister chromatids line up at the metaphase plate. The kinetochore breaks down and the sister chromatids separate. The nucleus re-forms and the cell divides.
- d. The kinetochore becomes attached to the mitotic spindle. Sister chromatids line up at the metaphase plate. The kinetochore breaks apart and the sister chromatids separate. The nucleus re-forms and the cell divides.

Solution:

[\[link\]](#) D. The kinetochore becomes attached to the mitotic spindle. Sister chromatids line up at the metaphase plate. The kinetochore breaks apart and the sister chromatids separate. The nucleus reforms and the cell divides.

Multiple Choice**Exercise:****Problem:**

Chromosomes are duplicated during what portion of the cell cycle?

- a. G_1 phase

- b. S phase
- c. prophase
- d. prometaphase

Solution:

B

Exercise:

Problem:

Separation of the sister chromatids is a characteristic of which stage of mitosis?

- a. prometaphase
- b. metaphase
- c. anaphase
- d. telophase

Solution:

C

Exercise:

Problem:

The individual chromosomes become visible with a light microscope during which stage of mitosis?

- a. prophase
- b. prometaphase
- c. metaphase
- d. anaphase

Solution:

A

Exercise:

Problem: What is necessary for a cell to pass the G₂ checkpoint?

- a. cell has reached a sufficient size
 - b. an adequate stockpile of nucleotides
 - c. accurate and complete DNA replication
 - d. proper attachment of mitotic spindle fibers to kinetochores
-

Solution:

C

Free Response

Exercise:

Problem:

Describe the similarities and differences between the cytokinesis mechanisms found in animal cells versus those in plant cells.

Solution:

There are very few similarities between animal cell and plant cell cytokinesis. In animal cells, a ring of actin fibers is formed around the periphery of the cell at the former metaphase plate. The actin ring contracts inward, pulling the plasma membrane toward the center of the cell until the cell is pinched in two. In plant cells, a new cell wall must be formed between the daughter cells. Because of the rigid cell walls of the parent cell, contraction of the middle of the cell is not possible. Instead, a cell plate is formed in the center of the cell at the former metaphase plate. The cell plate is formed from Golgi vesicles that contain enzymes, proteins, and glucose. The vesicles fuse and the enzymes build a new cell wall from the proteins and glucose. The cell

plate grows toward, and eventually fuses with, the cell wall of the parent cell.

Glossary

anaphase

the stage of mitosis during which sister chromatids are separated from each other

cell cycle

the ordered sequence of events that a cell passes through between one cell division and the next

cell cycle checkpoints

mechanisms that monitor the preparedness of a eukaryotic cell to advance through the various cell cycle stages

cell plate

a structure formed during plant-cell cytokinesis by Golgi vesicles fusing at the metaphase plate; will ultimately lead to formation of a cell wall to separate the two daughter cells

centriole

a paired rod-like structure constructed of microtubules at the center of each animal cell centrosome

cleavage furrow

a constriction formed by the actin ring during animal-cell cytokinesis that leads to cytoplasmic division

cytokinesis

the division of the cytoplasm following mitosis to form two daughter cells

G₀ phase

a cell-cycle phase distinct from the G₁ phase of interphase; a cell in G₀ is not preparing to divide

G₁ phase

(also, first gap) a cell-cycle phase; first phase of interphase centered on cell growth during mitosis

G₂ phase

(also, second gap) a cell-cycle phase; third phase of interphase where the cell undergoes the final preparations for mitosis

interphase

the period of the cell cycle leading up to mitosis; includes G₁, S, and G₂ phases; the interim between two consecutive cell divisions

kinetochore

a protein structure in the centromere of each sister chromatid that attracts and binds spindle microtubules during prometaphase

metaphase plate

the equatorial plane midway between two poles of a cell where the chromosomes align during metaphase

metaphase

the stage of mitosis during which chromosomes are lined up at the metaphase plate

mitosis

the period of the cell cycle at which the duplicated chromosomes are separated into identical nuclei; includes prophase, prometaphase, metaphase, anaphase, and telophase

mitotic phase

the period of the cell cycle when duplicated chromosomes are distributed into two nuclei and the cytoplasmic contents are divided; includes mitosis and cytokinesis

mitotic spindle

the microtubule apparatus that orchestrates the movement of chromosomes during mitosis

prometaphase

the stage of mitosis during which mitotic spindle fibers attach to kinetochores

prophase

the stage of mitosis during which chromosomes condense and the mitotic spindle begins to form

quiescent

describes a cell that is performing normal cell functions and has not initiated preparations for cell division

S phase

the second, or synthesis phase, of interphase during which DNA replication occurs

telophase

the stage of mitosis during which chromosomes arrive at opposite poles, decondense, and are surrounded by new nuclear envelopes

Bis2A 15.1 Cell Division

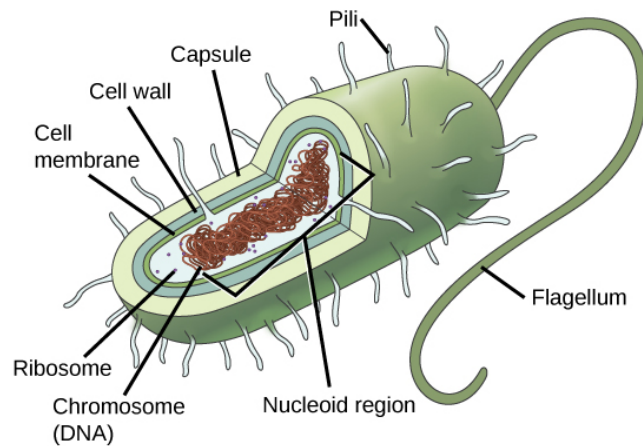
By the end of this section, you will be able to:

- Describe the structure of prokaryotic and eukaryotic genomes
- Distinguish between chromosomes, genes, and traits
- Describe the mechanisms of chromosome compaction

The continuity of life from one cell to another has its foundation in the reproduction of cells by way of the cell cycle. The **cell cycle** is an orderly sequence of events that describes the stages of a cell's life from the division of a single parent cell to the production of two new daughter cells. The mechanisms involved in the cell cycle are highly regulated.

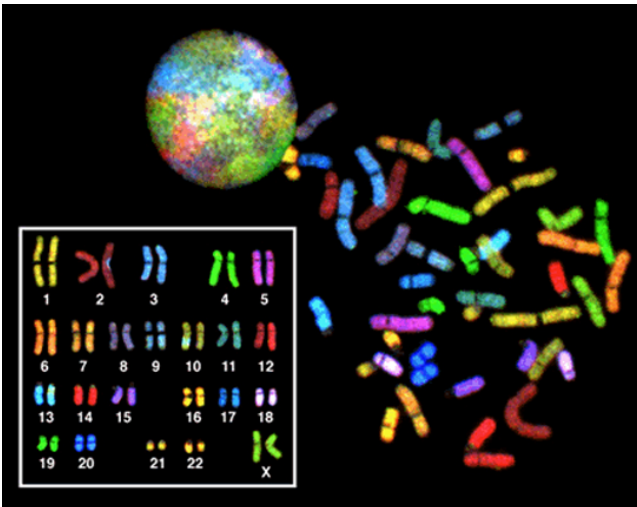
Genomic DNA

Before discussing the steps a cell must undertake to replicate, a deeper understanding of the structure and function of a cell's genetic information is necessary. A cell's DNA, packaged as a double-stranded DNA molecule, is called its **genome**. In prokaryotes, the genome is composed of a single, double-stranded DNA molecule in the form of a loop or circle ([\[link\]](#)). The region in the cell containing this genetic material is called a nucleoid. Some prokaryotes also have smaller loops of DNA called plasmids that are not essential for normal growth. Bacteria can exchange these plasmids with other bacteria, sometimes receiving beneficial new genes that the recipient can add to their chromosomal DNA. Antibiotic resistance is one trait that often spreads through a bacterial colony through plasmid exchange.



Prokaryotes, including bacteria and archaea, have a single, circular chromosome located in a central region called the nucleoid.

In eukaryotes, the genome consists of several double-stranded linear DNA molecules ([\[link\]](#)). Each species of eukaryotes has a characteristic number of chromosomes in the nuclei of its cells. Human body cells have 46 chromosomes, while human **gametes** (sperm or eggs) have 23 chromosomes each. A typical body cell, or somatic cell, contains two matched sets of chromosomes, a configuration known as **diploid**. The letter n is used to represent a single set of chromosomes; therefore, a diploid organism is designated $2n$. Human cells that contain one set of chromosomes are called gametes, or sex cells; these are eggs and sperm, and are designated $1n$, or **haploid**.



There are 23 pairs of homologous chromosomes in a female human somatic cell. The condensed chromosomes are viewed within the nucleus (top), removed from a cell in mitosis and spread out on a slide (right), and artificially arranged according to length (left); an arrangement like this is called a karyotype. In this image, the chromosomes were exposed to fluorescent stains for differentiation of the different chromosomes. A method of staining called “chromosome painting” employs fluorescent dyes that highlight chromosomes in different colors. (credit: National Human Genome Project/NIH)

Matched pairs of chromosomes in a diploid organism are called **homologous** (“same knowledge”) **chromosomes**. Homologous

chromosomes are the same length and have specific nucleotide segments called **genes** in exactly the same location, or **locus**. Genes, the functional units of chromosomes, determine specific characteristics by coding for specific proteins. Traits are the variations of those characteristics. For example, hair color is a characteristic with traits that are blonde, brown, or black.

Each copy of a homologous pair of chromosomes originates from a different parent; therefore, the genes themselves are not identical. The variation of individuals within a species is due to the specific combination of the genes inherited from both parents. Even a slightly altered sequence of nucleotides within a gene can result in an alternative trait. For example, there are three possible gene sequences on the human chromosome that code for blood type: sequence A, sequence B, and sequence O. Because all diploid human cells have two copies of the chromosome that determines blood type, the blood type (the trait) is determined by which two versions of the marker gene are inherited. It is possible to have two copies of the same gene sequence on both homologous chromosomes, with one on each (for example, AA, BB, or OO), or two different sequences, such as AB.

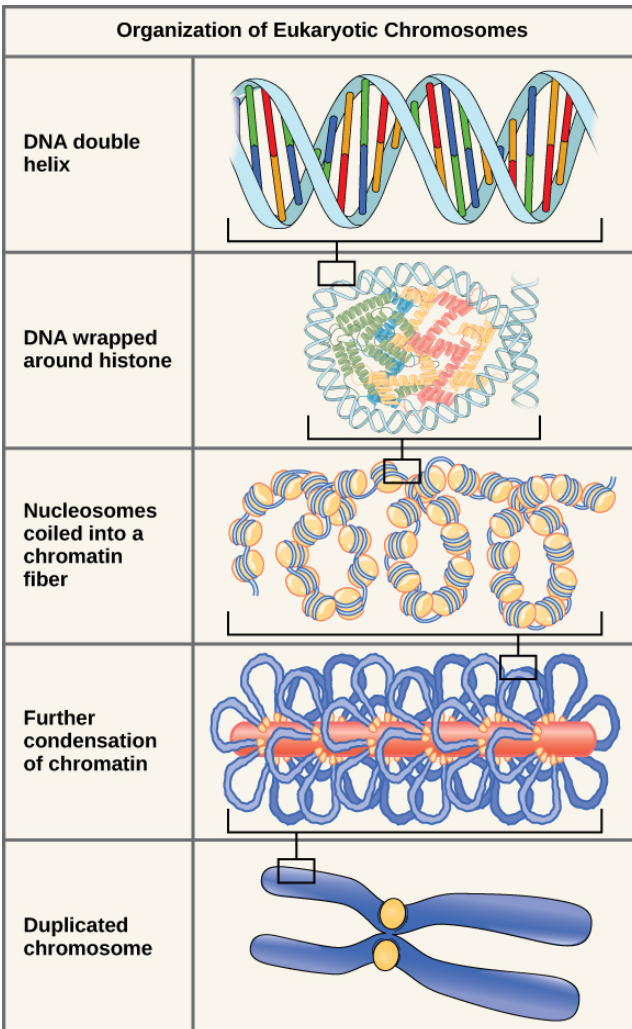
Minor variations of traits, such as blood type, eye color, and handedness, contribute to the natural variation found within a species. However, if the entire DNA sequence from any pair of human homologous chromosomes is compared, the difference is less than one percent. The sex chromosomes, X and Y, are the single exception to the rule of homologous chromosome uniformity: Other than a small amount of homology that is necessary to accurately produce gametes, the genes found on the X and Y chromosomes are different.

Eukaryotic Chromosomal Structure and Compaction

If the DNA from all 46 chromosomes in a human cell nucleus was laid out end to end, it would measure approximately two meters; however, its diameter would be only 2 nm. Considering that the size of a typical human cell is about 10 μm (100,000 cells lined up to equal one meter), DNA must be tightly packaged to fit in the cell's nucleus. At the same time, it must also be readily accessible for the genes to be expressed. During some stages

of the cell cycle, the long strands of DNA are condensed into compact chromosomes. There are a number of ways that chromosomes are compacted.

In the first level of compaction, short stretches of the DNA double helix wrap around a core of eight **histone proteins** at regular intervals along the entire length of the chromosome ([\[link\]](#)). The DNA-histone complex is called chromatin. The beadlike, histone DNA complex is called a **nucleosome**, and DNA connecting the nucleosomes is called linker DNA. A DNA molecule in this form is about seven times shorter than the double helix without the histones, and the beads are about 10 nm in diameter, in contrast with the 2-nm diameter of a DNA double helix. The next level of compaction occurs as the nucleosomes and the linker DNA between them are coiled into a 30-nm chromatin fiber. This coiling further shortens the chromosome so that it is now about 50 times shorter than the extended form. In the third level of packing, a variety of fibrous proteins is used to pack the chromatin. These fibrous proteins also ensure that each chromosome in a non-dividing cell occupies a particular area of the nucleus that does not overlap with that of any other chromosome (see the top image in [\[link\]](#)).



Double-stranded DNA wraps around histone proteins to form nucleosomes that have the appearance of “beads on a string.” The nucleosomes are coiled into a 30-nm chromatin fiber. When a cell undergoes mitosis, the chromosomes condense even further.

DNA replicates in the S phase of interphase. After replication, the chromosomes are composed of two linked sister **chromatids**. When fully

compact, the pairs of identically packed chromosomes are bound to each other by cohesin proteins. The connection between the sister chromatids is closest in a region called the **centromere**. The conjoined sister chromatids, with a diameter of about 1 μm , are visible under a light microscope. The centromeric region is highly condensed and thus will appear as a constricted area.

Note:

Link to Learning



[This animation](#) illustrates the different levels of chromosome packing.

Section Summary

Prokaryotes have a single circular chromosome composed of double-stranded DNA, whereas eukaryotes have multiple, linear chromosomes composed of chromatin surrounded by a nuclear membrane. The 46 chromosomes of human somatic cells are composed of 22 pairs of autosomes (matched pairs) and a pair of sex chromosomes, which may or may not be matched. This is the $2n$ or diploid state. Human gametes have 23 chromosomes or one complete set of chromosomes; a set of chromosomes is complete with either one of the sex chromosomes. This is the n or haploid state. Genes are segments of DNA that code for a specific protein. An organism's traits are determined by the genes inherited from each parent. Duplicated chromosomes are composed of two sister chromatids. Chromosomes are compacted using a variety of mechanisms

during certain stages of the cell cycle. Several classes of protein are involved in the organization and packing of the chromosomal DNA into a highly condensed structure. The condensing complex compacts chromosomes, and the resulting condensed structure is necessary for chromosomal segregation during mitosis.

Review Questions

Exercise:

Problem:

A diploid cell has _____ the number of chromosomes as a haploid cell.

- a. one-fourth
- b. half
- c. twice
- d. four times

Solution:

C

Exercise:

Problem:

An organism's traits are determined by the specific combination of inherited _____.

- a. cells.
- b. genes.
- c. proteins.
- d. chromatids.

Solution:

B

Exercise:

Problem:

The first level of DNA organization in a eukaryotic cell is maintained by which molecule?

- a. cohesin
- b. condensin
- c. chromatin
- d. histone

Solution:

D

Exercise:

Problem:

Identical copies of chromatin held together by cohesin at the centromere are called _____.

- a. histones.
- b. nucleosomes.
- c. chromatin.
- d. sister chromatids.

Solution:

D

Free Response

Exercise:

Problem:

Compare and contrast a human somatic cell to a human gamete.

Solution:

Human somatic cells have 46 chromosomes: 22 pairs and 2 sex chromosomes that may or may not form a pair. This is the $2n$ or diploid condition. Human gametes have 23 chromosomes, one each of 23 unique chromosomes, one of which is a sex chromosome. This is the n or haploid condition.

Exercise:**Problem:**

What is the relationship between a genome, chromosomes, and genes?

Solution:

The genome consists of the sum total of an organism's chromosomes. Each chromosome contains hundreds and sometimes thousands of genes, segments of DNA that code for a polypeptide or RNA, and a large amount of DNA with no known function.

Exercise:**Problem:**

Eukaryotic chromosomes are thousands of times longer than a typical cell. Explain how chromosomes can fit inside a eukaryotic nucleus.

Solution:

The DNA double helix is wrapped around histone proteins to form structures called nucleosomes. Nucleosomes and the linker DNA in between them are coiled into a 30-nm fiber. During cell division, chromatin is further condensed by packing proteins.

Glossary

cell cycle

ordered sequence of events that a cell passes through between one cell division and the next

centromere

region at which sister chromatids are bound together; a constricted area in condensed chromosomes

chromatid

single DNA molecule of two strands of duplicated DNA and associated proteins held together at the centromere

diploid

cell, nucleus, or organism containing two sets of chromosomes ($2n$)

gamete

haploid reproductive cell or sex cell (sperm, pollen grain, or egg)

gene

physical and functional unit of heredity, a sequence of DNA that codes for a protein.

genome

total genetic information of a cell or organism

haploid

cell, nucleus, or organism containing one set of chromosomes (n)

histone

one of several similar, highly conserved, low molecular weight, basic proteins found in the chromatin of all eukaryotic cells; associates with DNA to form nucleosomes

homologous chromosomes

chromosomes of the same morphology with genes in the same location; diploid organisms have pairs of homologous chromosomes

(homologs), with each homolog derived from a different parent

locus

position of a gene on a chromosome

nucleosome

subunit of chromatin composed of a short length of DNA wrapped around a core of histone proteins

Bis2A 15.2 Cell Growth and Division

By the end of this section, you will be able to:

- Describe the stages of the cell cycle
- Discuss how the cell cycle is regulated
- Describe the implications of losing control over the cell cycle
- Describe the stages of mitosis and cytokinesis, in order

So far in this chapter, you have read numerous times of the importance and prevalence of cell division. While there are a few cells in the body that do not undergo cell division (such as gametes, red blood cells, most neurons, and some muscle cells), most somatic cells divide regularly. A **somatic cell** is a general term for a body cell, and all human cells, except for the cells that produce eggs and sperm (which are referred to as germ cells), are somatic cells. Somatic cells contain *two* copies of each of their chromosomes (one copy received from each parent). A **homologous** pair of chromosomes is the two copies of a single chromosome found in each somatic cell. The human is a **diploid** organism, having 23 homologous pairs of chromosomes in each of the somatic cells. The condition of having pairs of chromosomes is known as diploidy.

Cells in the body replace themselves over the lifetime of a person. For example, the cells lining the gastrointestinal tract must be frequently replaced when constantly “worn off” by the movement of food through the gut. But what triggers a cell to divide, and how does it prepare for and complete cell division? The **cell cycle** is the sequence of events in the life of the cell from the moment it is created at the end of a previous cycle of cell division until it then divides itself, generating two new cells.

The Cell Cycle

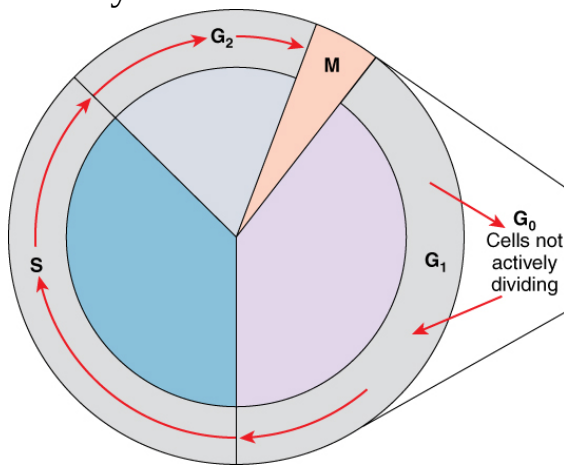
One “turn” or cycle of the cell cycle consists of two general phases: interphase, followed by mitosis and cytokinesis. **Interphase** is the period of the cell cycle during which the cell is not dividing. The majority of cells are in interphase most of the time. **Mitosis** is the division of genetic material, during which the cell nucleus breaks down and two new, fully functional,

nuclei are formed. **Cytokinesis** divides the cytoplasm into two distinctive cells.

Interphase

A cell grows and carries out all normal metabolic functions and processes in a period called G_1 ([link](#)). **G_1 phase** (gap 1 phase) is the first gap, or growth phase in the cell cycle. For cells that will divide again, G_1 is followed by replication of the DNA, during the S phase. The **S phase** (synthesis phase) is period during which a cell replicates its DNA.

Cell Cycle



The two major phases of the cell cycle include mitosis (cell division), and interphase, when the cell grows and performs all of its normal functions. Interphase is further subdivided into G_1 , S, and G_2 phases.

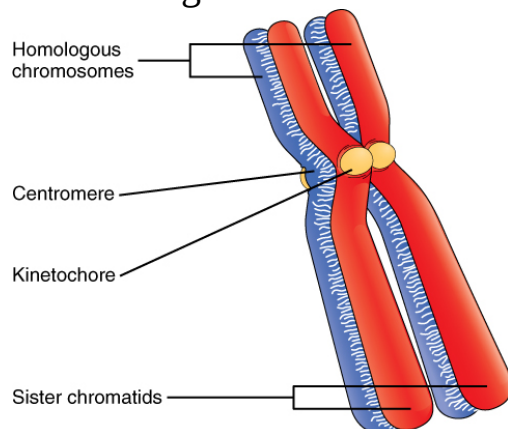
After the synthesis phase, the cell proceeds through the G_2 phase. The **G_2 phase** is a second gap phase, during which the cell continues to grow and makes the necessary preparations for mitosis. Between G_1 , S, and G_2

phases, cells will vary the most in their duration of the G₁ phase. It is here that a cell might spend a couple of hours, or many days. The S phase typically lasts between 8-10 hours and the G₂ phase approximately 5 hours. In contrast to these phases, the **G₀ phase** is a resting phase of the cell cycle. Cells that have temporarily stopped dividing and are resting (a common condition) and cells that have permanently ceased dividing (like nerve cells) are said to be in G₀.

The Structure of Chromosomes

Billions of cells in the human body divide every day. During the synthesis phase (S, for DNA synthesis) of interphase, the amount of DNA within the cell precisely doubles. Therefore, after DNA replication but before cell division, each cell actually contains *two* copies of each chromosome. Each copy of the chromosome is referred to as a **sister chromatid** and is physically bound to the other copy. The **centromere** is the structure that attaches one sister chromatid to another. Because a human cell has 46 chromosomes, during this phase, there are 92 chromatids (46×2) in the cell. Make sure not to confuse the concept of a pair of chromatids (one chromosome and its exact copy attached during mitosis) and a homologous pair of chromosomes (two paired chromosomes which were inherited separately, one from each parent) ([\[link\]](#)).

A Homologous Pair of Chromosomes with their Attached Sister Chromatids



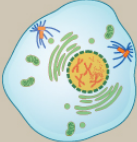
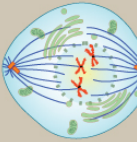
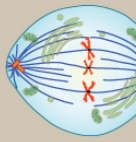
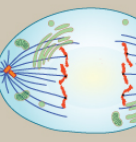
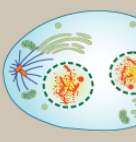
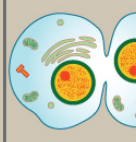
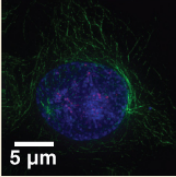
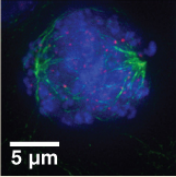
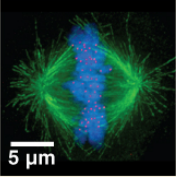
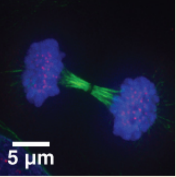
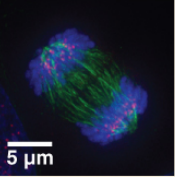
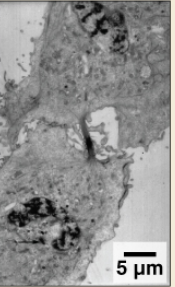
The red and blue colors
correspond to a

homologous pair of chromosomes. Each member of the pair was separately inherited from one parent. Each chromosome in the homologous pair is also bound to an identical sister chromatid, which is produced by DNA replication, and results in the familiar “X” shape.

Mitosis and Cytokinesis

The **mitotic phase** of the cell typically takes between 1 and 2 hours. During this phase, a cell undergoes two major processes. First, it completes mitosis, during which the contents of the nucleus are equitably pulled apart and distributed between its two halves. Cytokinesis then occurs, dividing the cytoplasm and cell body into two new cells. Mitosis is divided into four major stages that take place after interphase ([\[link\]](#)) and in the following order: prophase, metaphase, anaphase, and telophase. The process is then followed by cytokinesis.

Cell Division: Mitosis Followed by Cytokinesis

Prophase	Prometaphase	Metaphase	Anaphase	Telophase	Cytokinesis
					
<ul style="list-style-type: none"> Chromosomes condense and become visible Spindle fibers emerge from the centrosomes Nuclear envelope breaks down Centrosomes move toward opposite poles 	<ul style="list-style-type: none"> Chromosomes continue to condense Kinetochores appear at the centromeres Mitotic spindle microtubules attach to kinetochores 	<ul style="list-style-type: none"> Chromosomes are lined up at the metaphase plate Each sister chromatid is attached to a spindle fiber originating from opposite poles 	<ul style="list-style-type: none"> Centromeres split in two Sister chromatids (now called chromosomes) are pulled toward opposite poles Certain spindle fibers begin to elongate the cell 	<ul style="list-style-type: none"> Chromosomes arrive at opposite poles and begin to decondense Nuclear envelope material surrounds each set of chromosomes The mitotic spindle breaks down Spindle fibers continue to push poles apart 	<ul style="list-style-type: none"> Animal cells: a cleavage furrow separates the daughter cells Plant cells: a cell plate, the precursor to a new cell wall, separates the daughter cells
					

MITOSIS

The stages of cell division oversee the separation of identical genetic material into two new nuclei, followed by the division of the cytoplasm.

Prophase is the first phase of mitosis, during which the loosely packed chromatin coils and condenses into visible chromosomes. During prophase, each chromosome becomes visible with its identical partner attached, forming the familiar X-shape of sister chromatids. The nucleolus disappears early during this phase, and the nuclear envelope also disintegrates.

A major occurrence during prophase concerns a very important structure that contains the origin site for microtubule growth. Recall the cellular structures called centrioles that serve as origin points from which microtubules extend. These tiny structures also play a very important role

during mitosis. A **centrosome** is a pair of centrioles together. The cell contains two centrosomes side-by-side, which begin to move apart during prophase. As the centrosomes migrate to two different sides of the cell, microtubules begin to extend from each like long fingers from two hands extending toward each other. The **mitotic spindle** is the structure composed of the centrosomes and their emerging microtubules.

Near the end of prophase there is an invasion of the nuclear area by microtubules from the mitotic spindle. The nuclear membrane has disintegrated, and the microtubules attach themselves to the centromeres that adjoin pairs of sister chromatids. The **kinetochore** is a protein structure on the centromere that is the point of attachment between the mitotic spindle and the sister chromatids. This stage is referred to as late prophase or “prometaphase” to indicate the transition between prophase and metaphase.

Metaphase is the second stage of mitosis. During this stage, the sister chromatids, with their attached microtubules, line up along a linear plane in the middle of the cell. A metaphase plate forms between the centrosomes that are now located at either end of the cell. The **metaphase plate** is the name for the plane through the center of the spindle on which the sister chromatids are positioned. The microtubules are now poised to pull apart the sister chromatids and bring one from each pair to each side of the cell.

Anaphase is the third stage of mitosis. Anaphase takes place over a few minutes, when the pairs of sister chromatids are separated from one another, forming individual chromosomes once again. These chromosomes are pulled to opposite ends of the cell by their kinetochores, as the microtubules shorten. Each end of the cell receives one partner from each pair of sister chromatids, ensuring that the two new daughter cells will contain identical genetic material.

Telophase is the final stage of mitosis. Telophase is characterized by the formation of two new daughter nuclei at either end of the dividing cell. These newly formed nuclei surround the genetic material, which uncoils such that the chromosomes return to loosely packed chromatin. Nucleoli also reappear within the new nuclei, and the mitotic spindle breaks apart, each new cell receiving its own complement of DNA, organelles,

membranes, and centrioles. At this point, the cell is already beginning to split in half as cytokinesis begins.

The **cleavage furrow** is a contractile band made up of microfilaments that forms around the midline of the cell during cytokinesis. (Recall that microfilaments consist of actin.) This contractile band squeezes the two cells apart until they finally separate. Two new cells are now formed. One of these cells (the “stem cell”) enters its own cell cycle; able to grow and divide again at some future time. The other cell transforms into the functional cell of the tissue, typically replacing an “old” cell there.

Imagine a cell that completed mitosis but never underwent cytokinesis. In some cases, a cell may divide its genetic material and grow in size, but fail to undergo cytokinesis. This results in larger cells with more than one nucleus. Usually this is an unwanted aberration and can be a sign of cancerous cells.

Cell Cycle Control

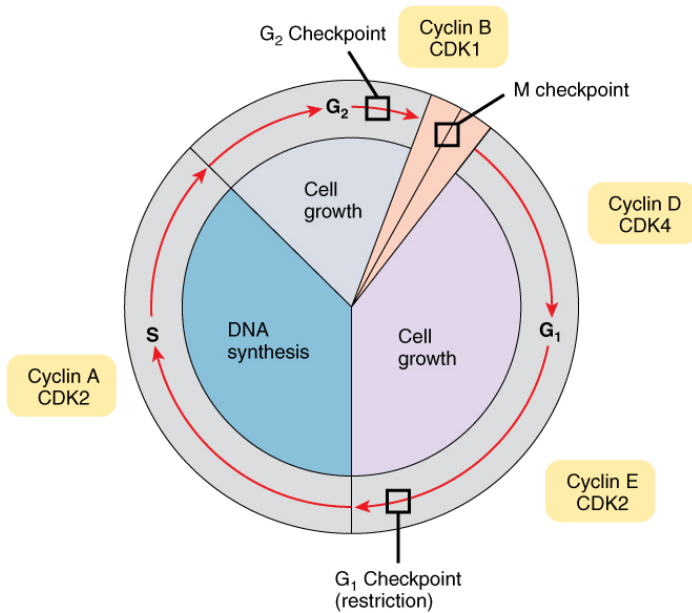
A very elaborate and precise system of regulation controls direct the way cells proceed from one phase to the next in the cell cycle and begin mitosis. The control system involves molecules within the cell as well as external triggers. These internal and external control triggers provide “stop” and “advance” signals for the cell. Precise regulation of the cell cycle is critical for maintaining the health of an organism, and loss of cell cycle control can lead to cancer.

Mechanisms of Cell Cycle Control

As the cell proceeds through its cycle, each phase involves certain processes that must be completed before the cell should advance to the next phase. A **checkpoint** is a point in the cell cycle at which the cycle can be signaled to move forward or stopped. At each of these checkpoints, different varieties of molecules provide the stop or go signals, depending on certain conditions within the cell. A **cyclin** is one of the primary classes of cell cycle control molecules ([\[link\]](#)). A **cyclin-dependent kinase (CDK)** is

one of a group of molecules that work together with cyclins to determine progression past cell checkpoints. By interacting with many additional molecules, these triggers push the cell cycle forward unless prevented from doing so by “stop” signals, if for some reason the cell is not ready. At the G_1 checkpoint, the cell must be ready for DNA synthesis to occur. At the G_2 checkpoint the cell must be fully prepared for mitosis. Even during mitosis, a crucial stop and go checkpoint in metaphase ensures that the cell is fully prepared to complete cell division. The metaphase checkpoint ensures that all sister chromatids are properly attached to their respective microtubules and lined up at the metaphase plate before the signal is given to separate them during anaphase.

Control of the Cell Cycle



Cells proceed through the cell cycle under the control of a variety of molecules, such as cyclins and cyclin-dependent kinases. These control molecules determine whether or not the cell is prepared to move into the following stage.

The Cell Cycle Out of Control: Implications

Most people understand that cancer or tumors are caused by abnormal cells that multiply continuously. If the abnormal cells continue to divide unstopped, they can damage the tissues around them, spread to other parts of the body, and eventually result in death. In healthy cells, the tight regulation mechanisms of the cell cycle prevent this from happening, while failures of cell cycle control can cause unwanted and excessive cell division. Failures of control may be caused by inherited genetic abnormalities that compromise the function of certain “stop” and “go” signals. Environmental insult that damages DNA can also cause dysfunction in those signals. Often, a combination of both genetic predisposition and environmental factors lead to cancer.

The process of a cell escaping its normal control system and becoming cancerous may actually happen throughout the body quite frequently. Fortunately, certain cells of the immune system are capable of recognizing cells that have become cancerous and destroying them. However, in certain cases the cancerous cells remain undetected and continue to proliferate. If the resulting tumor does not pose a threat to surrounding tissues, it is said to be benign and can usually be easily removed. If capable of damage, the tumor is considered malignant and the patient is diagnosed with cancer.

Note:

Homeostatic Imbalances

Cancer Arises from Homeostatic Imbalances

Cancer is an extremely complex condition, capable of arising from a wide variety of genetic and environmental causes. Typically, mutations or aberrations in a cell's DNA that compromise normal cell cycle control systems lead to cancerous tumors. Cell cycle control is an example of a homeostatic mechanism that maintains proper cell function and health. While progressing through the phases of the cell cycle, a large variety of intracellular molecules provide stop and go signals to regulate movement forward to the next phase. These signals are maintained in an intricate balance so that the cell only proceeds to the next phase when it is ready. This homeostatic control of the cell cycle can be thought of like a car's

cruise control. Cruise control will continually apply just the right amount of acceleration to maintain a desired speed, unless the driver hits the brakes, in which case the car will slow down. Similarly, the cell includes molecular messengers, such as cyclins, that push the cell forward in its cycle.

In addition to cyclins, a class of proteins that are encoded by genes called proto-oncogenes provide important signals that regulate the cell cycle and move it forward. Examples of proto-oncogene products include cell-surface receptors for growth factors, or cell-signaling molecules, two classes of molecules that can promote DNA replication and cell division. In contrast, a second class of genes known as tumor suppressor genes sends stop signals during a cell cycle. For example, certain protein products of tumor suppressor genes signal potential problems with the DNA and thus stop the cell from dividing, while other proteins signal the cell to die if it is damaged beyond repair. Some tumor suppressor proteins also signal a sufficient surrounding cellular density, which indicates that the cell need not presently divide. The latter function is uniquely important in preventing tumor growth: normal cells exhibit a phenomenon called “contact inhibition;” thus, extensive cellular contact with neighboring cells causes a signal that stops further cell division.

These two contrasting classes of genes, proto-oncogenes and tumor suppressor genes, are like the accelerator and brake pedal of the cell’s own “cruise control system,” respectively. Under normal conditions, these stop and go signals are maintained in a homeostatic balance. Generally speaking, there are two ways that the cell’s cruise control can lose control: a malfunctioning (overactive) accelerator, or a malfunctioning (underactive) brake. When compromised through a mutation, or otherwise altered, proto-oncogenes can be converted to oncogenes, which produce oncoproteins that push a cell forward in its cycle and stimulate cell division even when it is undesirable to do so. For example, a cell that should be programmed to self-destruct (a process called apoptosis) due to extensive DNA damage might instead be triggered to proliferate by an oncoprotein. On the other hand, a dysfunctional tumor suppressor gene may fail to provide the cell with a necessary stop signal, also resulting in unwanted cell division and proliferation.

A delicate homeostatic balance between the many proto-oncogenes and tumor suppressor genes delicately controls the cell cycle and ensures that

only healthy cells replicate. Therefore, a disruption of this homeostatic balance can cause aberrant cell division and cancerous growths.

Note:



Visit this [link](#) to learn about mitosis. Mitosis results in two identical diploid cells. What structures form during prophase?

Chapter Review

The life of a cell consists of stages that make up the cell cycle. After a cell is born, it passes through an interphase before it is ready to replicate itself and produce daughter cells. This interphase includes two gap phases (G_1 and G_2), as well as an S phase, during which its DNA is replicated in preparation for cell division. The cell cycle is under precise regulation by chemical messengers both inside and outside the cell that provide “stop” and “go” signals for movement from one phase to the next. Failures of these signals can result in cells that continue to divide uncontrollably, which can lead to cancer.

Once a cell has completed interphase and is ready for cell division, it proceeds through four separate stages of mitosis (prophase, metaphase, anaphase, and telophase). Telophase is followed by the division of the cytoplasm (cytokinesis), which generates two daughter cells. This process takes place in all normally dividing cells of the body except for the germ cells that produce eggs and sperm.

Interactive Link Questions

Exercise:

Problem:

Visit this [link](#) to learn about mitosis. Mitosis results in two identical diploid cells. What structures form during prophase?

Solution:

the spindle

Review Questions

Exercise:

Problem:

Which of the following phases is characterized by preparation for DNA synthesis?

- a. G_0
 - b. G_1
 - c. G_2
 - d. S
-

Solution:

B

Exercise:

Problem:

A mutation in the gene for a cyclin protein might result in which of the following?

- a. a cell with additional genetic material than normal

- b. cancer
- c. a cell with less genetic material than normal
- d. any of the above

Solution:

D

Exercise:

Problem: What is a primary function of tumor suppressor genes?

- a. stop all cells from dividing
- b. stop certain cells from dividing
- c. help oncogenes produce oncoproteins
- d. allow the cell to skip certain phases of the cell cycle

Solution:

B

Critical Thinking Questions

Exercise:

Problem:

What would happen if anaphase proceeded even though the sister chromatids were not properly attached to their respective microtubules and lined up at the metaphase plate?

Solution:

One or both of the new daughter cells would accidentally receive duplicate chromosomes and/or would be missing certain chromosomes.

Exercise:**Problem:**

What are cyclins and cyclin-dependent kinases, and how do they interact?

Solution:

A cyclin is one of the primary classes of cell cycle control molecules, while a cyclin-dependent kinase (is one of a group of molecules that work together with cyclins to determine progression past cell checkpoints. By interacting with many additional molecules, these triggers push the cell cycle forward unless prevented from doing so by “stop” signals, if for some reason the cell is not ready.

Glossary

anaphase

third stage of mitosis (and meiosis), during which sister chromatids separate into two new nuclear regions of a dividing cell

cell cycle

life cycle of a single cell, from its birth until its division into two new daughter cells

centromere

region of attachment for two sister chromatids

centrosome

cellular structure that organizes microtubules during cell division

checkpoint

progress point in the cell cycle during which certain conditions must be met in order for the cell to proceed to a subsequent phase

cleavage furrow

contractile ring that forms around a cell during cytokinesis that pinches the cell into two halves

cyclin

one of a group of proteins that function in the progression of the cell cycle

cyclin-dependent kinase (CDK)

one of a group of enzymes associated with cyclins that help them perform their functions

cytokinesis

final stage in cell division, where the cytoplasm divides to form two separate daughter cells

diploid

condition marked by the presence of a double complement of genetic material (two sets of chromosomes, one set inherited from each of two parents)

G₀ phase

phase of the cell cycle, usually entered from the G₁ phase; characterized by long or permanent periods where the cell does not move forward into the DNA synthesis phase

G₁ phase

first phase of the cell cycle, after a new cell is born

G₂ phase

third phase of the cell cycle, after the DNA synthesis phase

homologous

describes two copies of the same chromosome (not identical), one inherited from each parent

interphase

entire life cycle of a cell, excluding mitosis

kinetochore

region of a centromere where microtubules attach to a pair of sister chromatids

metaphase

second stage of mitosis (and meiosis), characterized by the linear alignment of sister chromatids in the center of the cell

metaphase plate

linear alignment of sister chromatids in the center of the cell, which takes place during metaphase

mitosis

division of genetic material, during which the cell nucleus breaks down and two new, fully functional, nuclei are formed

mitotic phase

phase of the cell cycle in which a cell undergoes mitosis

mitotic spindle

network of microtubules, originating from centrioles, that arranges and pulls apart chromosomes during mitosis

prophase

first stage of mitosis (and meiosis), characterized by breakdown of the nuclear envelope and condensing of the chromatin to form chromosomes

S phase

stage of the cell cycle during which DNA replication occurs

sister chromatid

one of a pair of identical chromosomes, formed during DNA replication

somatic cell

all cells of the body excluding gamete cells

telophase

final stage of mitosis (and meiosis), preceding cytokinesis,
characterized by the formation of two new daughter nuclei

Bis2A 15.3 Bacterial and Archaeal Cell Division

By the end of this section, you will be able to:

- Describe the process of binary fission in prokaryotes
- Explain how FtsZ and tubulin proteins are examples of homology

Prokaryotes, such as bacteria, propagate by binary fission. For unicellular organisms, cell division is the only method to produce new individuals. In both prokaryotic and eukaryotic cells, the outcome of cell reproduction is a pair of daughter cells that are genetically identical to the parent cell. In unicellular organisms, daughter cells are individuals.

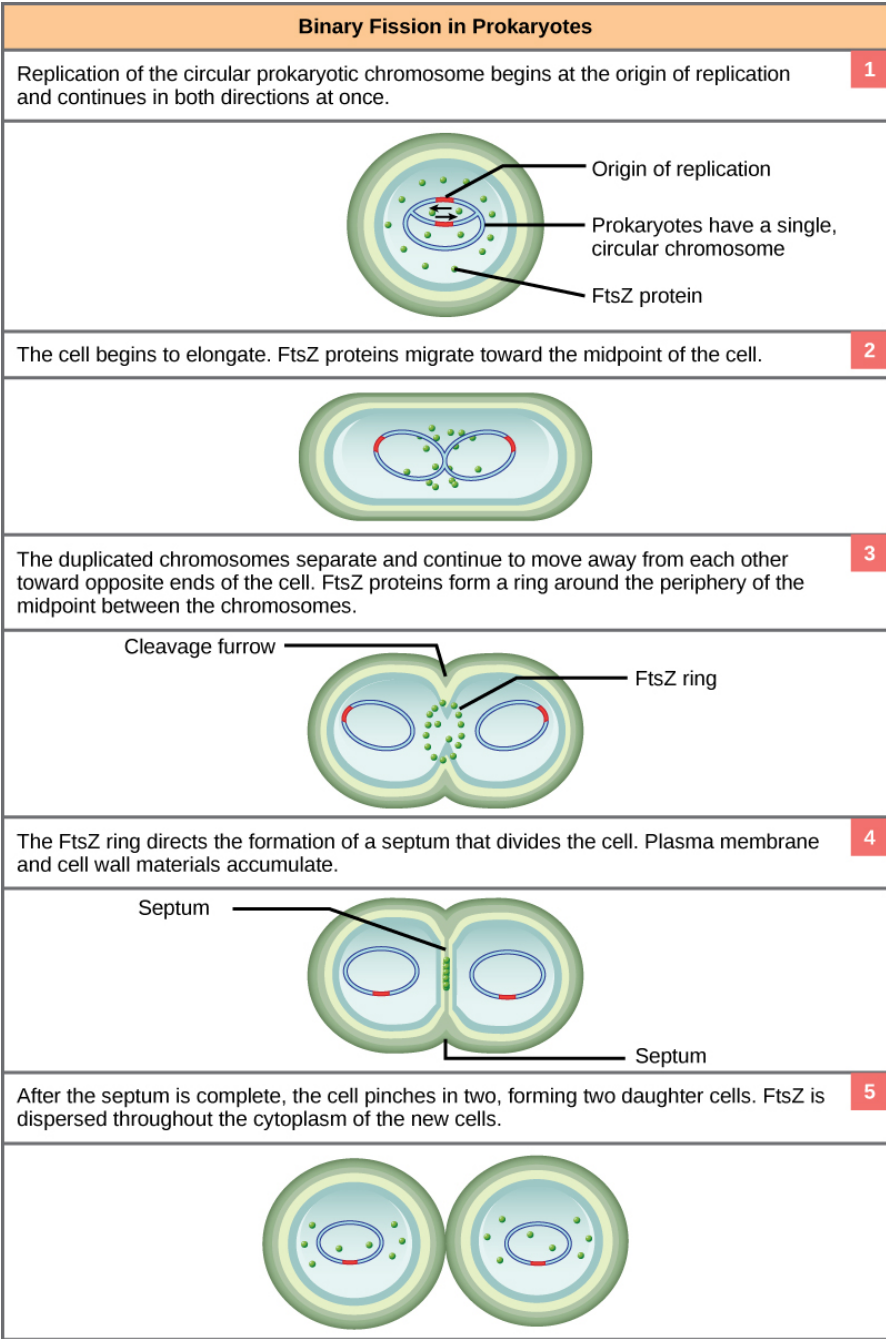
To achieve the outcome of cloned offspring, certain steps are essential. The genomic DNA must be replicated and then allocated into the daughter cells; the cytoplasmic contents must also be divided to give both new cells the machinery to sustain life. In bacterial cells, the genome consists of a single, circular DNA chromosome; therefore, the process of cell division is simplified. Karyokinesis is unnecessary because there is no nucleus and thus no need to direct one copy of the multiple chromosomes into each daughter cell. This type of cell division is called **binary (prokaryotic) fission**.

Binary Fission

Due to the relative simplicity of the prokaryotes, the cell division process, called binary fission, is a less complicated and much more rapid process than cell division in eukaryotes. The single, circular DNA chromosome of bacteria is not enclosed in a nucleus, but instead occupies a specific location, the nucleoid, within the cell ([\[link\]](#)). Although the DNA of the nucleoid is associated with proteins that aid in packaging the molecule into a compact size, there are no histone proteins and thus no nucleosomes in prokaryotes. The packing proteins of bacteria are, however, related to the cohesin and condensin proteins involved in the chromosome compaction of eukaryotes.

The bacterial chromosome is attached to the plasma membrane at about the midpoint of the cell. The starting point of replication, the **origin**, is close to the binding site of the chromosome to the plasma membrane ([\[link\]](#)). Replication of the DNA is bidirectional, moving away from the origin on both strands of the loop simultaneously. As the new double strands are

formed, each origin point moves away from the cell wall attachment toward the opposite ends of the cell. As the cell elongates, the growing membrane aids in the transport of the chromosomes. After the chromosomes have cleared the midpoint of the elongated cell, cytoplasmic separation begins. The formation of a ring composed of repeating units of a protein called **FtsZ** directs the partition between the nucleoids. Formation of the FtsZ ring triggers the accumulation of other proteins that work together to recruit new membrane and cell wall materials to the site. A **septum** is formed between the nucleoids, extending gradually from the periphery toward the center of the cell. When the new cell walls are in place, the daughter cells separate.



These images show the steps of binary fission in prokaryotes. (credit: modification of work by “Mcstrother”/Wikimedia Commons)

Note:**Evolution Connection****Mitotic Spindle Apparatus**

The precise timing and formation of the mitotic spindle is critical to the success of eukaryotic cell division. Prokaryotic cells, on the other hand, do not undergo karyokinesis and therefore have no need for a mitotic spindle. However, the FtsZ protein that plays such a vital role in prokaryotic cytokinesis is structurally and functionally very similar to tubulin, the building block of the microtubules that make up the mitotic spindle fibers that are necessary for eukaryotes. FtsZ proteins can form filaments, rings, and other three-dimensional structures that resemble the way tubulin forms microtubules, centrioles, and various cytoskeletal components. In addition, both FtsZ and tubulin employ the same energy source, GTP (guanosine triphosphate), to rapidly assemble and disassemble complex structures. FtsZ and tubulin are homologous structures derived from common evolutionary origins. In this example, FtsZ is the ancestor protein to tubulin (a modern protein). While both proteins are found in extant organisms, tubulin function has evolved and diversified tremendously since evolving from its FtsZ prokaryotic origin. A survey of mitotic assembly components found in present-day unicellular eukaryotes reveals crucial intermediary steps to the complex membrane-enclosed genomes of multicellular eukaryotes ([\[link\]](#)).

Cell Division Apparatus among Various Organisms

	Structure of genetic material	Division of nuclear material	Separation of daughter cells

Cell Division Apparatus among Various Organisms			
	Structure of genetic material	Division of nuclear material	Separation of daughter cells
Prokaryotes	There is no nucleus. The single, circular chromosome exists in a region of cytoplasm called the nucleoid.	Occurs through binary fission. As the chromosome is replicated, the two copies move to opposite ends of the cell by an unknown mechanism.	FtsZ proteins assemble into a ring that pinches the cell in two.
Some protists	Linear chromosomes exist in the nucleus.	Chromosomes attach to the nuclear envelope, which remains intact. The mitotic spindle passes through the envelope and elongates the cell. No centrioles exist.	Microfilaments form a cleavage furrow that pinches the cell in two.

Cell Division Apparatus among Various Organisms			
	Structure of genetic material	Division of nuclear material	Separation of daughter cells
Other protists	Linear chromosomes exist in the nucleus.	A mitotic spindle forms from the centrioles and passes through the nuclear membrane, which remains intact. Chromosomes attach to the mitotic spindle, which separates the chromosomes and elongates the cell.	Microfilaments form a cleavage furrow that pinches the cell in two.

Cell Division Apparatus among Various Organisms			
	Structure of genetic material	Division of nuclear material	Separation of daughter cells
Animal cells	Linear chromosomes exist in the nucleus.	A mitotic spindle forms from the centrosomes. The nuclear envelope dissolves. Chromosomes attach to the mitotic spindle, which separates the chromosomes and elongates the cell.	Microfilaments form a cleavage furrow that pinches the cell in two.

Section Summary

In both prokaryotic and eukaryotic cell division, the genomic DNA is replicated and then each copy is allocated into a daughter cell. In addition, the cytoplasmic contents are divided evenly and distributed to the new cells. However, there are many differences between prokaryotic and eukaryotic cell division. Bacteria have a single, circular DNA chromosome but no nucleus. Therefore, mitosis is not necessary in bacterial cell division. Bacterial cytokinesis is directed by a ring composed of a protein called FtsZ. Ingrowth of membrane and cell wall material from the periphery of the cells

results in the formation of a septum that eventually constructs the separate cell walls of the daughter cells.

Review Questions

Exercise:

Problem:

Which eukaryotic cell cycle event is missing in binary fission?

- a. cell growth
- b. DNA duplication
- c. karyokinesis
- d. cytokinesis

Solution:

C

Exercise:

Problem:

FtsZ proteins direct the formation of a _____ that will eventually form the new cell walls of the daughter cells.

- a. contractile ring
- b. cell plate
- c. cytoskeleton
- d. septum

Solution:

B

Free Response

Exercise:

Problem:

Name the common components of eukaryotic cell division and binary fission.

Solution:

The common components of eukaryotic cell division and binary fission are DNA duplication, segregation of duplicated chromosomes, and division of the cytoplasmic contents.

Exercise:

Problem:

Describe how the duplicated bacterial chromosomes are distributed into new daughter cells without the direction of the mitotic spindle.

Solution:

As the chromosome is being duplicated, each origin moves away from the starting point of replication. The chromosomes are attached to the cell membrane via proteins; the growth of the membrane as the cell elongates aids in their movement.

Glossary

binary fission

prokaryotic cell division process

FtsZ

tubulin-like protein component of the prokaryotic cytoskeleton that is important in prokaryotic cytokinesis (name origin: **F**ilamenting **t**emperature-sensitive mutant **Z**)

origin

(also, ORI) region of the prokaryotic chromosome where replication begins (origin of replication)

septum

structure formed in a bacterial cell as a precursor to the separation of the cell into two daughter cells

Bis2A 16.0 Introduction to Meiosis

class="introduction"

Each of us,
like these
other large
multicellula
r organisms,
begins life
as a
fertilized
egg. After
trillions of
cell
divisions,
each of us
develops
into a
complex,
multicellula
r organism.
(credit a:
modificatio
n of work
by Frank
Wouters;
credit b:
modificatio
n of work
by Ken
Cole,
USGS;
credit c:
modificatio
n of work
by Martin
Pettitt)



(a)

(b)

(c)

The ability to reproduce *in kind* is a basic characteristic of all living things. *In kind* means that the offspring of any organism closely resembles its parent or parents. Hippopotamuses give birth to hippopotamus calves; Monterey pine trees produce seeds from which Monterey pine seedlings emerge; and adult flamingos lay eggs that hatch into flamingo chicks. *In kind* does not generally mean *exactly the same*. While many single-celled organisms and a few multicellular organisms can produce genetically identical clones of themselves through mitotic cell division, many single-celled organisms and most multicellular organisms reproduce regularly using another method.

Sexual reproduction is the production by parents of haploid cells and the fusion of a haploid cell from each parent to form a single, unique diploid cell. In multicellular organisms, the new diploid cell will then undergo mitotic cell divisions to develop into an adult organism. A type of cell division called meiosis leads to the haploid cells that are part of the sexual reproductive cycle. Sexual reproduction, specifically meiosis and fertilization, introduces variation into offspring that may account for the evolutionary success of sexual reproduction. The vast majority of eukaryotic organisms can or must employ some form of meiosis and fertilization to reproduce.

Bis2A 16.1 Meiosis

By the end of this section, you will be able to:

- Describe the behavior of chromosomes during meiosis
- Describe cellular events during meiosis
- Explain the differences between meiosis and mitosis
- Explain the mechanisms within meiosis that generate genetic variation among the products of meiosis

Sexual reproduction requires **fertilization**, the union of two cells from two individual organisms. If those two cells each contain one set of chromosomes, then the resulting cell contains two sets of chromosomes. Haploid cells contain one set of chromosomes. Cells containing two sets of chromosomes are called diploid. The number of sets of chromosomes in a cell is called its ploidy level. If the reproductive cycle is to continue, then the diploid cell must somehow reduce its number of chromosome sets before fertilization can occur again, or there will be a continual doubling in the number of chromosome sets in every generation. So, in addition to fertilization, sexual reproduction includes a nuclear division that reduces the number of chromosome sets.

Most animals and plants are diploid, containing two sets of chromosomes. In each **somatic cell** of the organism (all cells of a multicellular organism except the gametes or reproductive cells), the nucleus contains two copies of each chromosome, called homologous chromosomes. Somatic cells are sometimes referred to as “body” cells. Homologous chromosomes are matched pairs containing the same genes in identical locations along their length. Diploid organisms inherit one copy of each homologous chromosome from each parent; all together, they are considered a full set of chromosomes. Haploid cells, containing a single copy of each homologous chromosome, are found only within structures that give rise to either gametes or spores. **Spores** are haploid cells that can produce a haploid organism or can fuse with another spore to form a diploid cell. All animals and most plants produce eggs and sperm, or gametes. Some plants and all fungi produce spores.

The nuclear division that forms haploid cells, which is called **meiosis**, is related to mitosis. As you have learned, mitosis is the part of a cell

reproduction cycle that results in identical daughter nuclei that are also genetically identical to the original parent nucleus. In mitosis, both the parent and the daughter nuclei are at the same ploidy level—diploid for most plants and animals. Meiosis employs many of the same mechanisms as mitosis. However, the starting nucleus is always diploid and the nuclei that result at the end of a meiotic cell division are haploid. To achieve this reduction in chromosome number, meiosis consists of one round of chromosome duplication and two rounds of nuclear division. Because the events that occur during each of the division stages are analogous to the events of mitosis, the same stage names are assigned. However, because there are two rounds of division, the major process and the stages are designated with a “I” or a “II.” Thus, **meiosis I** is the first round of meiotic division and consists of prophase I, prometaphase I, and so on. **Meiosis II**, in which the second round of meiotic division takes place, includes prophase II, prometaphase II, and so on.

Meiosis I

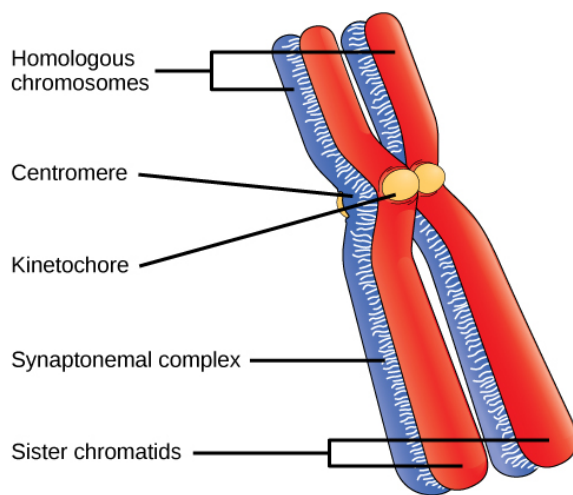
Meiosis is preceded by an interphase consisting of the G_1 , S, and G_2 phases, which are nearly identical to the phases preceding mitosis. The G_1 phase, which is also called the first gap phase, is the first phase of the interphase and is focused on cell growth. The S phase is the second phase of interphase, during which the DNA of the chromosomes is replicated. Finally, the G_2 phase, also called the second gap phase, is the third and final phase of interphase; in this phase, the cell undergoes the final preparations for meiosis.

During DNA duplication in the S phase, each chromosome is replicated to produce two identical copies, called sister chromatids, that are held together at the centromere by **cohesin** proteins. Cohesin holds the chromatids together until anaphase II. The centrosomes, which are the structures that organize the microtubules of the meiotic spindle, also replicate. This prepares the cell to enter prophase I, the first meiotic phase.

Prophase I

Early in prophase I, before the chromosomes can be seen clearly microscopically, the homologous chromosomes are attached at their tips to the nuclear envelope by proteins. As the nuclear envelope begins to break down, the proteins associated with homologous chromosomes bring the pair close to each other. Recall that, in mitosis, homologous chromosomes do not pair together. In mitosis, homologous chromosomes line up end-to-end so that when they divide, each daughter cell receives a sister chromatid from both members of the homologous pair. The **synaptonemal complex**, a lattice of proteins between the homologous chromosomes, first forms at specific locations and then spreads to cover the entire length of the chromosomes. The tight pairing of the homologous chromosomes is called **synapsis**. In synapsis, the genes on the chromatids of the homologous chromosomes are aligned precisely with each other. The synaptonemal complex supports the exchange of chromosomal segments between non-sister homologous chromatids, a process called crossing over. Crossing over can be observed visually after the exchange as **chiasmata** (singular = chiasma) ([link](#)).

In species such as humans, even though the X and Y sex chromosomes are not homologous (most of their genes differ), they have a small region of homology that allows the X and Y chromosomes to pair up during prophase I. A partial synaptonemal complex develops only between the regions of homology.

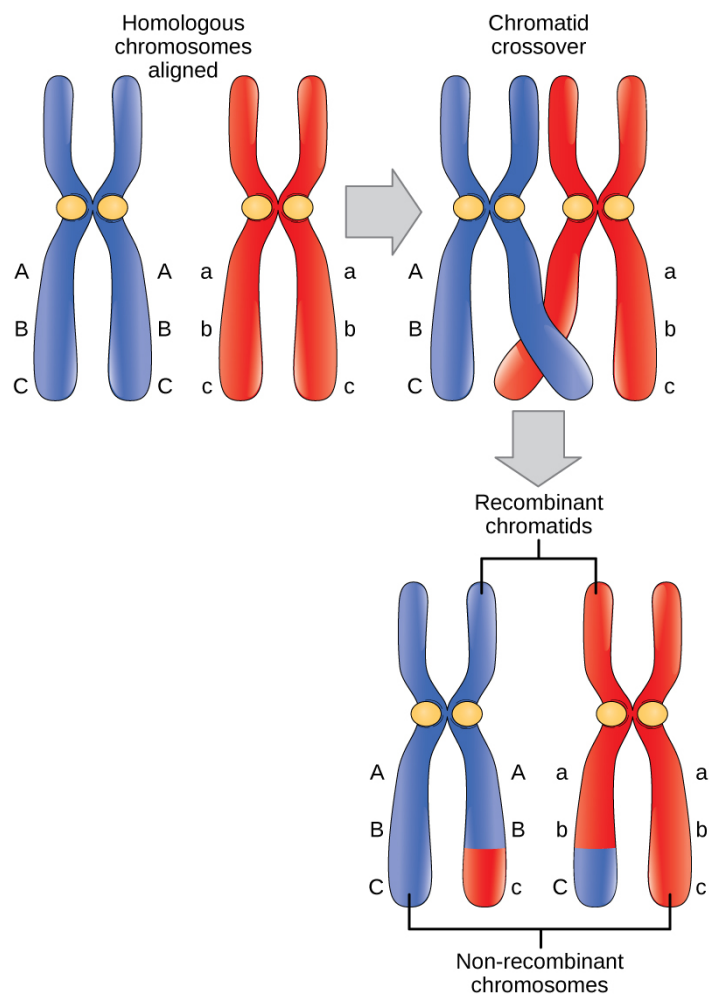


Early in prophase I, homologous chromosomes come together to form a synapse. The chromosomes are bound tightly together and in perfect alignment by a protein lattice called a synaptonemal complex and by cohesin proteins at the centromere.

Located at intervals along the synaptonemal complex are large protein assemblies called **recombination nodules**. These assemblies mark the points of later chiasmata and mediate the multistep process of **crossover**—or genetic recombination—between the non-sister chromatids. Near the recombination nodule on each chromatid, the double-stranded DNA is cleaved, the cut ends are modified, and a new connection is made between the non-sister chromatids. As prophase I progresses, the synaptonemal complex begins to break down and the chromosomes begin to condense. When the synaptonemal complex is gone, the homologous chromosomes remain attached to each other at the centromere and at chiasmata. The chiasmata remain until anaphase I. The number of chiasmata varies according to the species and the length of the chromosome. There must be at least one chiasma per chromosome for proper separation of homologous chromosomes during meiosis I, but there may be as many as 25. Following crossover, the synaptonemal complex breaks down and the cohesin connection between homologous pairs is also removed. At the end of prophase I, the pairs are held together only at the chiasmata ([\[link\]](#)) and are called **tetrads** because the four sister chromatids of each pair of homologous chromosomes are now visible.

The crossover events are the first source of genetic variation in the nuclei produced by meiosis. A single crossover event between homologous non-sister chromatids leads to a reciprocal exchange of equivalent DNA between a maternal chromosome and a paternal chromosome. Now, when that sister chromatid is moved into a gamete cell it will carry some DNA from one parent of the individual and some DNA from the other parent. The

sister recombinant chromatid has a combination of maternal and paternal genes that did not exist before the crossover. Multiple crossovers in an arm of the chromosome have the same effect, exchanging segments of DNA to create recombinant chromosomes.



Crossover occurs between non-sister chromatids of homologous chromosomes. The result is an exchange of genetic material between homologous chromosomes.

Prometaphase I

The key event in prometaphase I is the attachment of the spindle fiber microtubules to the kinetochore proteins at the centromeres. Kinetochore proteins are multiprotein complexes that bind the centromeres of a chromosome to the microtubules of the mitotic spindle. Microtubules grow from centrosomes placed at opposite poles of the cell. The microtubules move toward the middle of the cell and attach to one of the two fused homologous chromosomes. The microtubules attach at each chromosome's kinetochores. With each member of the homologous pair attached to opposite poles of the cell, in the next phase, the microtubules can pull the homologous pair apart. A spindle fiber that has attached to a kinetochore is called a kinetochore microtubule. At the end of prometaphase I, each tetrad is attached to microtubules from both poles, with one homologous chromosome facing each pole. The homologous chromosomes are still held together at chiasmata. In addition, the nuclear membrane has broken down entirely.

Metaphase I

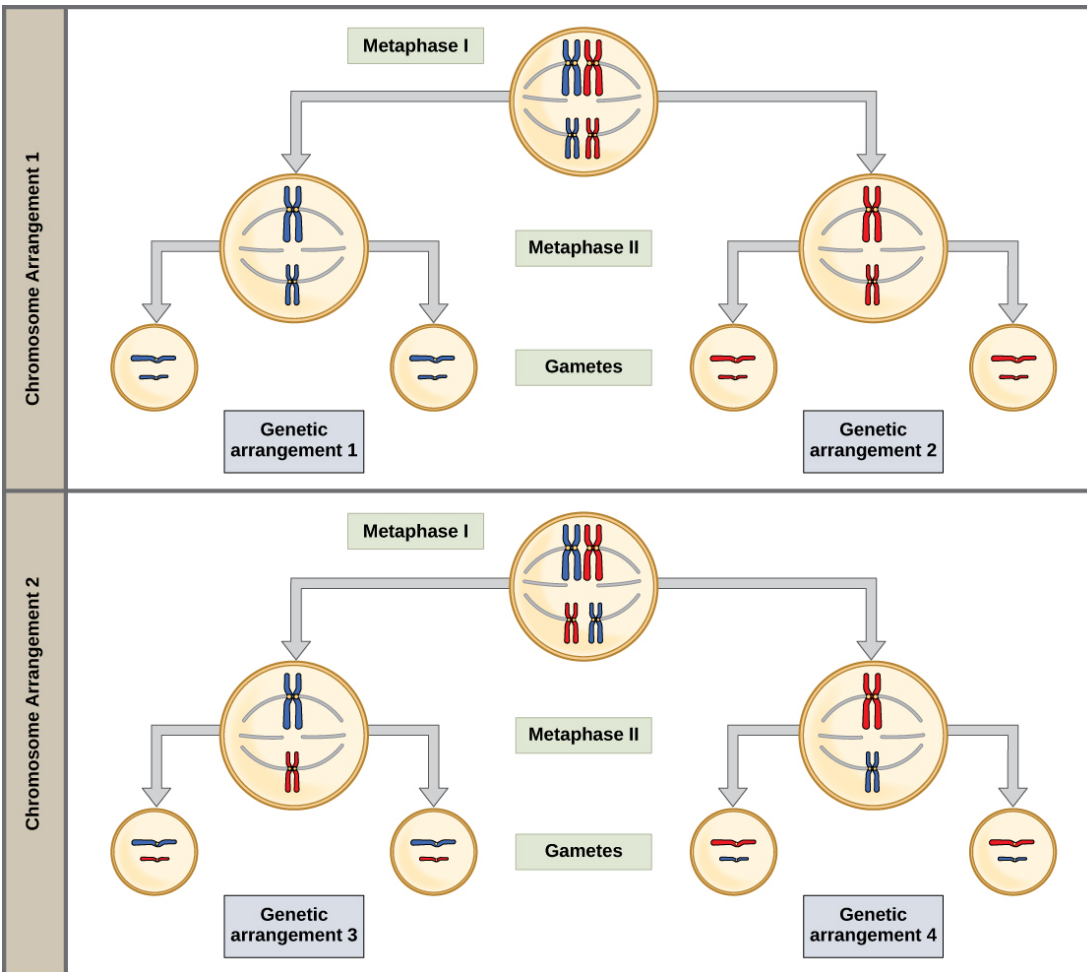
During metaphase I, the homologous chromosomes are arranged in the center of the cell with the kinetochores facing opposite poles. The homologous pairs orient themselves randomly at the equator. For example, if the two homologous members of chromosome 1 are labeled a and b, then the chromosomes could line up a-b, or b-a. This is important in determining the genes carried by a gamete, as each will only receive one of the two homologous chromosomes. Recall that homologous chromosomes are not identical. They contain slight differences in their genetic information, causing each gamete to have a unique genetic makeup.

This randomness is the physical basis for the creation of the second form of genetic variation in offspring. Consider that the homologous chromosomes of a sexually reproducing organism are originally inherited as two separate sets, one from each parent. Using humans as an example, one set of 23 chromosomes is present in the egg donated by the mother. The father provides the other set of 23 chromosomes in the sperm that fertilizes the

egg. Every cell of the multicellular offspring has copies of the original two sets of homologous chromosomes. In prophase I of meiosis, the homologous chromosomes form the tetrads. In metaphase I, these pairs line up at the midway point between the two poles of the cell to form the metaphase plate. Because there is an equal chance that a microtubule fiber will encounter a maternally or paternally inherited chromosome, the arrangement of the tetrads at the metaphase plate is random. Any maternally inherited chromosome may face either pole. Any paternally inherited chromosome may also face either pole. The orientation of each tetrad is independent of the orientation of the other 22 tetrads.

This event—the random (or independent) assortment of homologous chromosomes at the metaphase plate—is the second mechanism that introduces variation into the gametes or spores. In each cell that undergoes meiosis, the arrangement of the tetrads is different. The number of variations is dependent on the number of chromosomes making up a set. There are two possibilities for orientation at the metaphase plate; the possible number of alignments therefore equals $2n$, where n is the number of chromosomes per set. Humans have 23 chromosome pairs, which results in over eight million (2^{23}) possible genetically-distinct gametes. This number does not include the variability that was previously created in the sister chromatids by crossover. Given these two mechanisms, it is highly unlikely that any two haploid cells resulting from meiosis will have the same genetic composition ([link](#)).

To summarize the genetic consequences of meiosis I, the maternal and paternal genes are recombined by crossover events that occur between each homologous pair during prophase I. In addition, the random assortment of tetrads on the metaphase plate produces a unique combination of maternal and paternal chromosomes that will make their way into the gametes.



Random, independent assortment during metaphase I can be demonstrated by considering a cell with a set of two chromosomes ($n = 2$). In this case, there are two possible arrangements at the equatorial plane in metaphase I. The total possible number of different gametes is $2n$, where n equals the number of chromosomes in a set. In this example, there are four possible genetic combinations for the gametes. With $n = 23$ in human cells, there are over 8 million possible combinations of paternal and maternal chromosomes.

Anaphase I

In anaphase I, the microtubules pull the linked chromosomes apart. The sister chromatids remain tightly bound together at the centromere. The chiasmata are broken in anaphase I as the microtubules attached to the fused kinetochores pull the homologous chromosomes apart ([link](#)).

Telophase I and Cytokinesis

In telophase, the separated chromosomes arrive at opposite poles. The remainder of the typical telophase events may or may not occur, depending on the species. In some organisms, the chromosomes decondense and nuclear envelopes form around the chromatids in telophase I. In other organisms, cytokinesis—the physical separation of the cytoplasmic components into two daughter cells—occurs without reformation of the nuclei. In nearly all species of animals and some fungi, cytokinesis separates the cell contents via a cleavage furrow (constriction of the actin ring that leads to cytoplasmic division). In plants, a cell plate is formed during cell cytokinesis by Golgi vesicles fusing at the metaphase plate. This cell plate will ultimately lead to the formation of cell walls that separate the two daughter cells.

Two haploid cells are the end result of the first meiotic division. The cells are haploid because at each pole, there is just one of each pair of the homologous chromosomes. Therefore, only one full set of the chromosomes is present. This is why the cells are considered haploid—there is only one chromosome set, even though each homolog still consists of two sister chromatids. Recall that sister chromatids are merely duplicates of one of the two homologous chromosomes (except for changes that occurred during crossing over). In meiosis II, these two sister chromatids will separate, creating four haploid daughter cells.

Note:

[Link to Learning](#)



Review the process of meiosis, observing how chromosomes align and migrate, at [Meiosis: An Interactive Animation](#).

Meiosis II

In some species, cells enter a brief interphase, or **interkinesis**, before entering meiosis II. Interkinesis lacks an S phase, so chromosomes are not duplicated. The two cells produced in meiosis I go through the events of meiosis II in synchrony. During meiosis II, the sister chromatids within the two daughter cells separate, forming four new haploid gametes. The mechanics of meiosis II is similar to mitosis, except that each dividing cell has only one set of homologous chromosomes. Therefore, each cell has half the number of sister chromatids to separate out as a diploid cell undergoing mitosis.

Prophase II

If the chromosomes decondensed in telophase I, they condense again. If nuclear envelopes were formed, they fragment into vesicles. The centrosomes that were duplicated during interkinesis move away from each other toward opposite poles, and new spindles are formed.

Prometaphase II

The nuclear envelopes are completely broken down, and the spindle is fully formed. Each sister chromatid forms an individual kinetochore that attaches

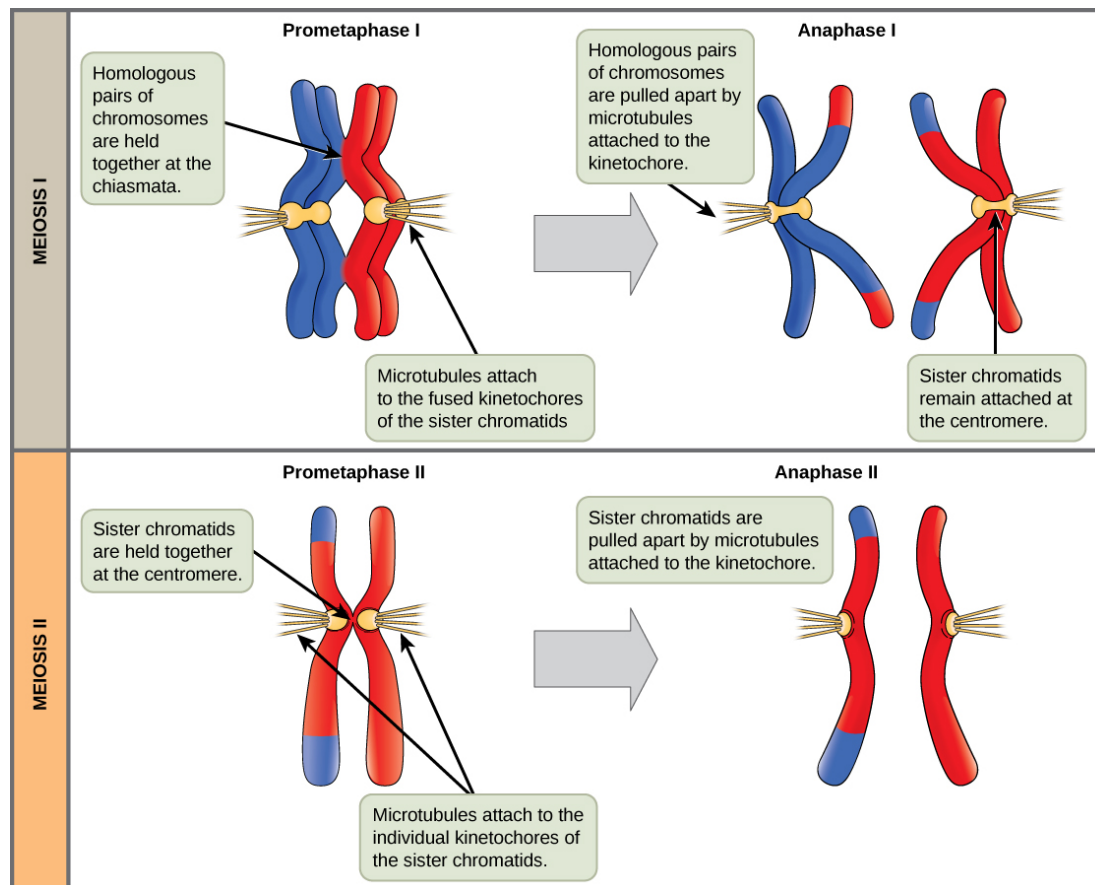
to microtubules from opposite poles.

Metaphase II

The sister chromatids are maximally condensed and aligned at the equator of the cell.

Anaphase II

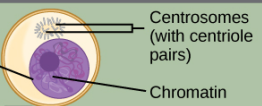
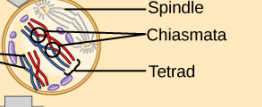
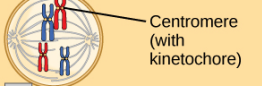
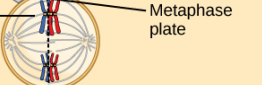



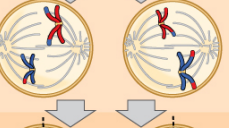

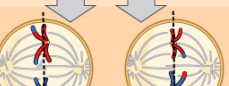
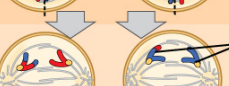
The sister chromatids are pulled apart by the kinetochore microtubules and move toward opposite poles. Non-kinetochore microtubules elongate the cell.



The process of chromosome alignment differs between meiosis I and meiosis II. In prometaphase I, microtubules attach to the fused kinetochores of homologous chromosomes, and the homologous chromosomes are arranged at the midpoint of the cell in metaphase I. In anaphase I, the homologous chromosomes are separated. In prometaphase II, microtubules attach to the kinetochores of sister chromatids, and the sister chromatids are arranged at the midpoint of the cells in metaphase II. In anaphase II, the sister chromatids are separated.

Telophase II and Cytokinesis

The chromosomes arrive at opposite poles and begin to decondense. Nuclear envelopes form around the chromosomes. Cytokinesis separates the two cells into four unique haploid cells. At this point, the newly formed nuclei are both haploid. The cells produced are genetically unique because of the random assortment of paternal and maternal homologs and because of the recombining of maternal and paternal segments of chromosomes (with their sets of genes) that occurs during crossover. The entire process of meiosis is outlined in [\[link\]](#).

Stage	Event	Outcome
INTERPHASE	S phase 	Chromosomes are duplicated during interphase. The resulting sister chromatids are held together at the centromere. The centrosomes are also duplicated.
	Prophase I 	Chromosomes condense, and the nuclear envelope fragments. Homologous chromosomes bind firmly together along their length, forming a tetrad. Chiasmata form between non-sister chromatids. Crossing over occurs at the chiasmata. Spindle fibers emerge from the centrosomes.
MEIOSIS I	Prometaphase I 	Homologous chromosomes are attached to spindle microtubules at the fused kinetochore shared by the sister chromatids. Chromosomes continue to condense, and the nuclear envelope completely disappears.
	Metaphase I 	Homologous chromosomes randomly assemble at the metaphase plate, where they have been maneuvered into place by the microtubules.
	Anaphase I 	Spindle microtubules pull the homologous chromosomes apart. The sister chromatids are still attached at the centromere.
	Telophase I and Cytokinesis 	Sister chromatids arrive at the poles of the cell and begin to decondense. A nuclear envelope forms around each nucleus and the cytoplasm is divided by a cleavage furrow. The result is two haploid cells. Each cell contains one duplicated copy of each homologous chromosome pair.
	Prophase II 	Sister chromatids condense. A new spindle begins to form. The nuclear envelope starts to fragment.
MEIOSIS II	Prometaphase II 	The nuclear envelope disappears, and the spindle fibers engage the individual kinetochores on the sister chromatids.
	Metaphase II 	Sister chromatids line up at the metaphase plate.
	Anaphase II 	Sister chromatids are pulled apart by the shortening of the kinetochore microtubules. Non-kinetochore microtubules lengthen the cell.
	Telophase II and Cytokinesis 	Chromosomes arrive at the poles of the cell and decondense. Nuclear envelopes surround the four nuclei. Cleavage furrows divide the two cells into four haploid cells.
	Haploid daughter cells	

An animal cell with a diploid number of four ($2n = 4$) proceeds through the stages of meiosis to form four haploid daughter cells.

Comparing Meiosis and Mitosis

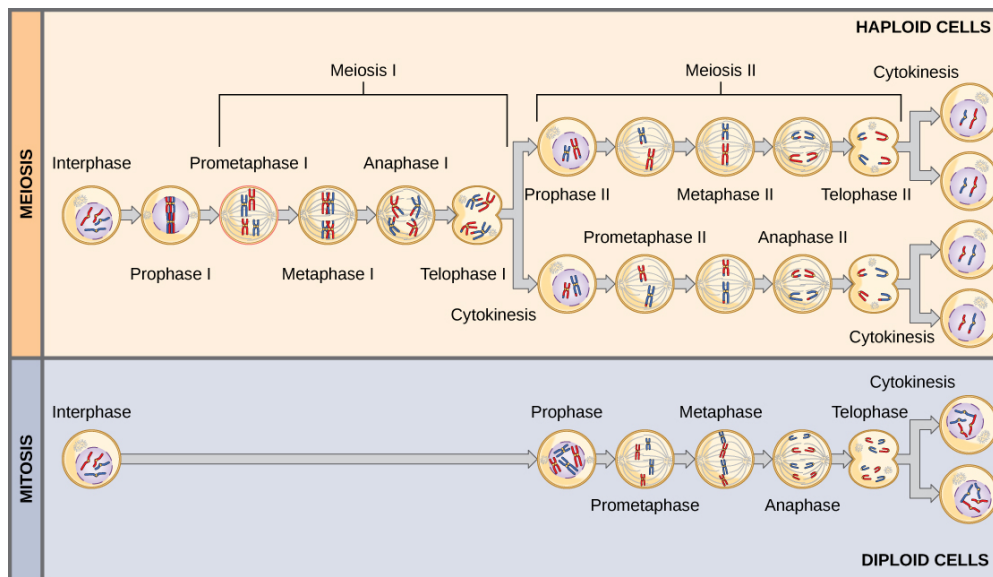
Mitosis and meiosis are both forms of division of the nucleus in eukaryotic cells. They share some similarities, but also exhibit distinct differences that lead to very different outcomes ([link](#)). Mitosis is a single nuclear division that results in two nuclei that are usually partitioned into two new cells. The nuclei resulting from a mitotic division are genetically identical to the original nucleus. They have the same number of sets of chromosomes, one set in the case of haploid cells and two sets in the case of diploid cells. In most plants and all animal species, it is typically diploid cells that undergo mitosis to form new diploid cells. In contrast, meiosis consists of two nuclear divisions resulting in four nuclei that are usually partitioned into four new cells. The nuclei resulting from meiosis are not genetically identical and they contain one chromosome set only. This is half the number of chromosome sets in the original cell, which is diploid.

The main differences between mitosis and meiosis occur in meiosis I, which is a very different nuclear division than mitosis. In meiosis I, the homologous chromosome pairs become associated with each other, are bound together with the synaptonemal complex, develop chiasmata and undergo crossover between sister chromatids, and line up along the metaphase plate in tetrads with kinetochore fibers from opposite spindle poles attached to each kinetochore of a homolog in a tetrad. All of these events occur only in meiosis I.

When the chiasmata resolve and the tetrad is broken up with the homologs moving to one pole or another, the ploidy level—the number of sets of chromosomes in each future nucleus—has been reduced from two to one. For this reason, meiosis I is referred to as a **reduction division**. There is no such reduction in ploidy level during mitosis.

Meiosis II is much more analogous to a mitotic division. In this case, the duplicated chromosomes (only one set of them) line up on the metaphase plate with divided kinetochores attached to kinetochore fibers from opposite poles. During anaphase II, as in mitotic anaphase, the kinetochores divide and one sister chromatid—now referred to as a chromosome—is pulled to one pole while the other sister chromatid is pulled to the other pole. If it

were not for the fact that there had been crossover, the two products of each individual meiosis II division would be identical (like in mitosis). Instead, they are different because there has always been at least one crossover per chromosome. Meiosis II is not a reduction division because although there are fewer copies of the genome in the resulting cells, there is still one set of chromosomes, as there was at the end of meiosis I.



						OUTCOME
PROCESS	DNA synthesis	Synapsis of homologous chromosomes	Crossover	Homologous chromosomes line up at metaphase plate	Sister chromatids line up at metaphase plate	Number and genetic composition of daughter cells
MEIOSIS	Occurs in S phase of interphase	During prophase I	During prophase I	During metaphase I	During metaphase II	Four haploid cells at the end of meiosis II
MITOSIS	Occurs in S phase of interphase	Does not occur in mitosis	Does not occur in mitosis	Does not occur in mitosis	During metaphase	Two diploid cells at the end of mitosis

Meiosis and mitosis are both preceded by one round of DNA replication; however, meiosis includes two nuclear divisions. The four daughter cells resulting from meiosis are haploid and genetically distinct. The daughter cells resulting from mitosis are diploid and identical to the parent cell.

Note:**Evolution Connection****The Mystery of the Evolution of Meiosis**

Some characteristics of organisms are so widespread and fundamental that it is sometimes difficult to remember that they evolved like other simpler traits. Meiosis is such an extraordinarily complex series of cellular events that biologists have had trouble hypothesizing and testing how it may have evolved. Although meiosis is inextricably entwined with sexual reproduction and its advantages and disadvantages, it is important to separate the questions of the evolution of meiosis and the evolution of sex, because early meiosis may have been advantageous for different reasons than it is now. Thinking outside the box and imagining what the early benefits from meiosis might have been is one approach to uncovering how it may have evolved.

Meiosis and mitosis share obvious cellular processes and it makes sense that meiosis evolved from mitosis. The difficulty lies in the clear differences between meiosis I and mitosis. Adam Wilkins and Robin Holliday^[footnote] summarized the unique events that needed to occur for the evolution of meiosis from mitosis. These steps are homologous chromosome pairing, crossover exchanges, sister chromatids remaining attached during anaphase, and suppression of DNA replication in interphase. They argue that the first step is the hardest and most important, and that understanding how it evolved would make the evolutionary process clearer. They suggest genetic experiments that might shed light on the evolution of synapsis.

Adam S. Wilkins and Robin Holliday, “The Evolution of Meiosis from Mitosis,” *Genetics* 181 (2009): 3–12.

There are other approaches to understanding the evolution of meiosis in progress. Different forms of meiosis exist in single-celled protists. Some appear to be simpler or more “primitive” forms of meiosis. Comparing the meiotic divisions of different protists may shed light on the evolution of meiosis. Marilee Ramesh and colleagues^[footnote] compared the genes involved in meiosis in protists to understand when and where meiosis might have evolved. Although research is still ongoing, recent scholarship

into meiosis in protists suggests that some aspects of meiosis may have evolved later than others. This kind of genetic comparison can tell us what aspects of meiosis are the oldest and what cellular processes they may have borrowed from in earlier cells.

Marilee A. Ramesh, Shehre-Banoo Malik and John M. Logsdon, Jr, “A Phylogenetic Inventory of Meiotic Genes: Evidence for Sex in *Giardia* and an Early Eukaryotic Origin of Meiosis,” *Current Biology* 15 (2005):185–91.

Note:

Link to Learning



Click through the steps of this interactive animation to compare the meiotic process of cell division to that of mitosis: [How Cells Divide](#).

Section Summary

Sexual reproduction requires that diploid organisms produce haploid cells that can fuse during fertilization to form diploid offspring. As with mitosis, DNA replication occurs prior to meiosis during the S-phase of the cell cycle. Meiosis is a series of events that arrange and separate chromosomes and chromatids into daughter cells. During the interphases of meiosis, each chromosome is duplicated. In meiosis, there are two rounds of nuclear division resulting in four nuclei and usually four daughter cells, each with half the number of chromosomes as the parent cell. The first separates homologs, and the second—like mitosis—separates chromatids into individual chromosomes. During meiosis, variation in the daughter nuclei is

introduced because of crossover in prophase I and random alignment of tetrads at metaphase I. The cells that are produced by meiosis are genetically unique.

Meiosis and mitosis share similarities, but have distinct outcomes. Mitotic divisions are single nuclear divisions that produce daughter nuclei that are genetically identical and have the same number of chromosome sets as the original cell. Meiotic divisions include two nuclear divisions that produce four daughter nuclei that are genetically different and have one chromosome set instead of the two sets of chromosomes in the parent cell. The main differences between the processes occur in the first division of meiosis, in which homologous chromosomes are paired and exchange non-sister chromatid segments. The homologous chromosomes separate into different nuclei during meiosis I, causing a reduction of ploidy level in the first division. The second division of meiosis is more similar to a mitotic division, except that the daughter cells do not contain identical genomes because of crossover.

Review Questions

Exercise:

Problem: Meiosis produces _____ daughter cells.

- a. two haploid
- b. two diploid
- c. four haploid
- d. four diploid

Solution:

C

Exercise:

Problem: What structure is most important in forming the tetrads?

- a. centromere
- b. synaptonemal complex
- c. chiasma
- d. kinetochore

Solution:

B

Exercise:

Problem:

At which stage of meiosis are sister chromatids separated from each other?

- a. prophase I
- b. prophase II
- c. anaphase I
- d. anaphase II

Solution:

D

Exercise:

Problem:

At metaphase I, homologous chromosomes are connected only at what structures?

- a. chiasmata
- b. recombination nodules
- c. microtubules
- d. kinetochores

Solution:

A

Exercise:

Problem: Which of the following is *not* true in regard to crossover?

- a. Spindle microtubules guide the transfer of DNA across the synaptonemal complex.
- b. Non-sister chromatids exchange genetic material.
- c. Chiasmata are formed.
- d. Recombination nodules mark the crossover point.

Solution:

C

Exercise:

Problem:

What phase of mitotic interphase is missing from meiotic interkinesis?

- a. G₀ phase
- b. G₁ phase
- c. S phase
- d. G₂ phase

Solution:

C

Exercise:

Problem: The part of meiosis that is similar to mitosis is _____.

- a. meiosis I
- b. anaphase I
- c. meiosis II

d. interkinesis

Solution:

C

Exercise:

Problem:

If a muscle cell of a typical organism has 32 chromosomes, how many chromosomes will be in a gamete of that same organism?

- a. 8
- b. 16
- c. 32
- d. 64

Solution:

B

Free Response

Exercise:

Problem: Describe the process that results in the formation of a tetrad.

Solution:

During the meiotic interphase, each chromosome is duplicated. The sister chromatids that are formed during synthesis are held together at the centromere region by cohesin proteins. All chromosomes are attached to the nuclear envelope by their tips. As the cell enters prophase I, the nuclear envelope begins to fragment, and the proteins holding homologous chromosomes locate each other. The four sister

chromatids align lengthwise, and a protein lattice called the synaptonemal complex is formed between them to bind them together. The synaptonemal complex facilitates crossover between non-sister chromatids, which is observed as chiasmata along the length of the chromosome. As prophase I progresses, the synaptonemal complex breaks down and the sister chromatids become free, except where they are attached by chiasmata. At this stage, the four chromatids are visible in each homologous pairing and are called a tetrad.

Exercise:

Problem:

Explain how the random alignment of homologous chromosomes during metaphase I contributes to the variation in gametes produced by meiosis.

Solution:

Random alignment leads to new combinations of traits. The chromosomes that were originally inherited by the gamete-producing individual came equally from the egg and the sperm. In metaphase I, the duplicated copies of these maternal and paternal homologous chromosomes line up across the center of the cell. The orientation of each tetrad is random. There is an equal chance that the maternally derived chromosomes will be facing either pole. The same is true of the paternally derived chromosomes. The alignment should occur differently in almost every meiosis. As the homologous chromosomes are pulled apart in anaphase I, any combination of maternal and paternal chromosomes will move toward each pole. The gametes formed from these two groups of chromosomes will have a mixture of traits from the individual's parents. Each gamete is unique.

Exercise:

Problem:

What is the function of the fused kinetochore found on sister chromatids in prometaphase I?

Solution:

In metaphase I, the homologous chromosomes line up at the metaphase plate. In anaphase I, the homologous chromosomes are pulled apart and move to opposite poles. Sister chromatids are not separated until meiosis II. The fused kinetochore formed during meiosis I ensures that each spindle microtubule that binds to the tetrad will attach to both sister chromatids.

Exercise:**Problem:**

In a comparison of the stages of meiosis to the stages of mitosis, which stages are unique to meiosis and which stages have the same events in both meiosis and mitosis?

Solution:

All of the stages of meiosis I, except possibly telophase I, are unique because homologous chromosomes are separated, not sister chromatids. In some species, the chromosomes do not decondense and the nuclear envelopes do not form in telophase I. All of the stages of meiosis II have the same events as the stages of mitosis, with the possible exception of prophase II. In some species, the chromosomes are still condensed and there is no nuclear envelope. Other than this, all processes are the same.

Glossary**chiasmata**

(singular, *chiasma*) the structure that forms at the crossover points after genetic material is exchanged

cohesin

proteins that form a complex that seals sister chromatids together at their centromeres until anaphase II of meiosis

crossover

exchange of genetic material between non-sister chromatids resulting in chromosomes that incorporate genes from both parents of the organism

fertilization

union of two haploid cells from two individual organisms

interkinesis

(also, *interphase II*) brief period of rest between meiosis I and meiosis II

meiosis

a nuclear division process that results in four haploid cells

meiosis I

first round of meiotic cell division; referred to as reduction division because the ploidy level is reduced from diploid to haploid

meiosis II

second round of meiotic cell division following meiosis I; sister chromatids are separated into individual chromosomes, and the result is four unique haploid cells

recombination nodules

protein assemblies formed on the synaptonemal complex that mark the points of crossover events and mediate the multistep process of genetic recombination between non-sister chromatids

reduction division

nuclear division that produces daughter nuclei each having one-half as many chromosome sets as the parental nucleus; meiosis I is a reduction division

somatic cell

all the cells of a multicellular organism except the gametes or reproductive cells

spore

haploid cell that can produce a haploid multicellular organism or can fuse with another spore to form a diploid cell

synapsis

formation of a close association between homologous chromosomes during prophase I

synaptonemal complex

protein lattice that forms between homologous chromosomes during prophase I, supporting crossover

tetrad

two duplicated homologous chromosomes (four chromatids) bound together by chiasmata during prophase I

Bis2A 16.2 Errors in Meiosis

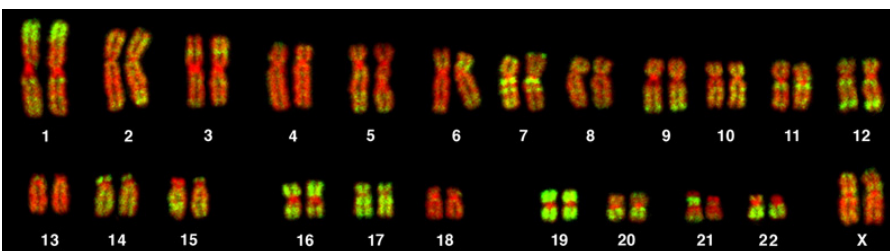
By the end of this section, you will be able to:

- Explain how nondisjunction leads to disorders in chromosome number
- Describe how errors in chromosome structure occur through inversions and translocations

Inherited disorders can arise when chromosomes behave abnormally during meiosis. Chromosome disorders can be divided into two categories: abnormalities in chromosome number and chromosome structural rearrangements. Because even small segments of chromosomes can span many genes, chromosomal disorders are characteristically dramatic and often fatal.

Disorders in Chromosome Number

The isolation and microscopic observation of chromosomes forms the basis of cytogenetics and is the primary method by which clinicians detect chromosomal abnormalities in humans. A **karyotype** is the number and appearance of chromosomes, including their length, banding pattern, and centromere position. To obtain a view of an individual's karyotype, cytologists photograph the chromosomes and then cut and paste each chromosome into a chart, or **karyogram** ([link](#)).



This karyogram shows the chromosomes of a female human immune cell during mitosis. (credit: Andreas Bolzer, et al)

Note:**Careers in Action****Geneticists Use Karyograms to Identify Chromosomal Aberrations**

The karyotype is a method by which traits characterized by chromosomal abnormalities can be identified from a single cell. To observe an individual's karyotype, a person's cells (like white blood cells) are first collected from a blood sample or other tissue. In the laboratory, the isolated cells are stimulated to begin actively dividing. A chemical is then applied to the cells to arrest mitosis during metaphase. The cells are then fixed to a slide.

The geneticist then stains chromosomes with one of several dyes to better visualize the distinct and reproducible banding patterns of each chromosome pair. Following staining, chromosomes are viewed using bright-field microscopy. An experienced cytogeneticist can identify each band. In addition to the banding patterns, chromosomes are further identified on the basis of size and centromere location. To obtain the classic depiction of the karyotype in which homologous pairs of chromosomes are aligned in numerical order from longest to shortest, the geneticist obtains a digital image, identifies each chromosome, and manually arranges the chromosomes into this pattern ([\[link\]](#)).

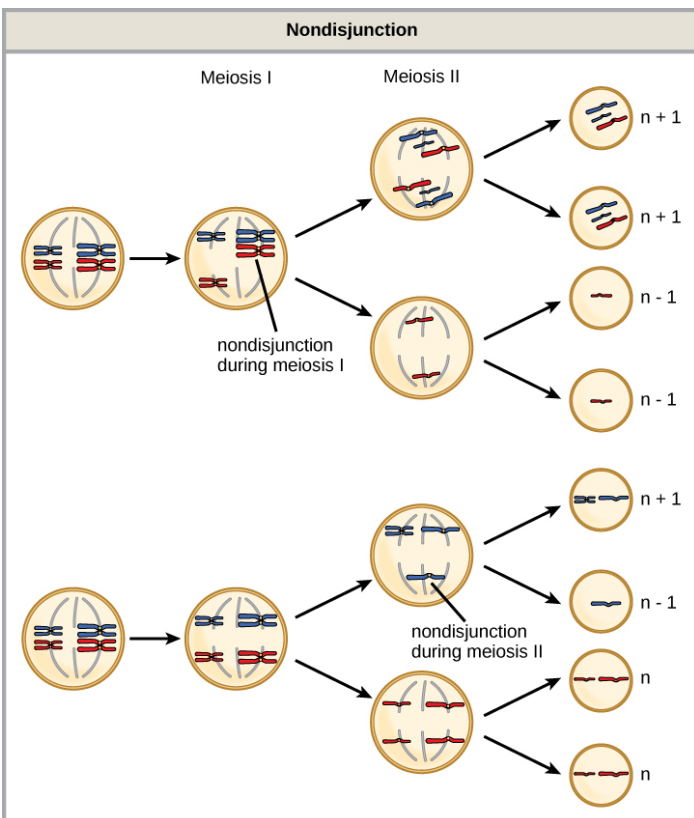
At its most basic, the karyogram may reveal genetic abnormalities in which an individual has too many or too few chromosomes per cell. Examples of this are Down syndrome, which is identified by a third copy of chromosome 21, and Turner syndrome, which is characterized by the presence of only one X chromosome in women instead of two. Geneticists can also identify large deletions or insertions of DNA. For instance, Jacobsen syndrome, which involves distinctive facial features as well as heart and bleeding defects, is identified by a deletion on chromosome 11. Finally, the karyotype can pinpoint **translocations**, which occur when a segment of genetic material breaks from one chromosome and reattaches to another chromosome or to a different part of the same chromosome. Translocations are implicated in certain cancers, including chronic myelogenous leukemia.

By observing a karyogram, geneticists can actually visualize the chromosomal composition of an individual to confirm or predict genetic abnormalities in offspring even before birth.

Nondisjunctions, Duplications, and Deletions

Of all the chromosomal disorders, abnormalities in chromosome number are the most easily identifiable from a karyogram. Disorders of chromosome number include the duplication or loss of entire chromosomes, as well as changes in the number of complete sets of chromosomes. They are caused by **nondisjunction**, which occurs when pairs of homologous chromosomes or sister chromatids fail to separate during meiosis. The risk of nondisjunction increases with the age of the parents.

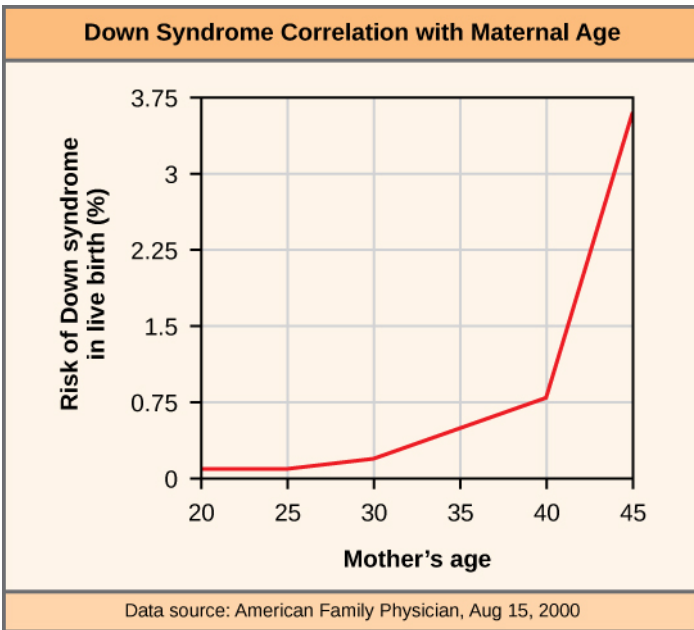
Nondisjunction can occur during either meiosis I or II, with different results ([link](#)). If homologous chromosomes fail to separate during meiosis I, the result is two gametes that lack that chromosome and two gametes with two copies of the chromosome. If sister chromatids fail to separate during meiosis II, the result is one gamete that lacks that chromosome, two normal gametes with one copy of the chromosome, and one gamete with two copies of the chromosome.



Following meiosis, each gamete has one copy of each chromosome.

Nondisjunction occurs when homologous chromosomes (meiosis I) or sister chromatids (meiosis II) fail to separate during meiosis.

An individual with the appropriate number of chromosomes for their species is called **euploid**; in humans, euploidy corresponds to 22 pairs of **autosomes** and one pair of sex chromosomes. An individual with an error in chromosome number is described as **aneuploid**, a term that includes **monosomy** (loss of one chromosome) or **trisomy** (gain of an extraneous chromosome). Monosomic human zygotes missing any one copy of an autosome invariably fail to develop to birth because they have only one copy of essential genes. Most autosomal trisomies also fail to develop to birth; however, duplications of some of the smaller chromosomes (13, 15, 18, 21, or 22) can result in offspring that survive for several weeks to many years. Trisomic individuals suffer from a different type of genetic imbalance: an excess in gene dose. Cell functions are calibrated to the amount of gene product produced by two copies (doses) of each gene; adding a third copy (dose) disrupts this balance. The most common trisomy is that of chromosome 21, which leads to Down syndrome. Individuals with this inherited disorder have characteristic physical features and developmental delays in growth and cognition. The incidence of Down syndrome is correlated with maternal age, such that older women are more likely to give birth to children with Down syndrome ([link](#)).



The incidence of having a fetus with trisomy 21 increases dramatically with maternal age.

Note:
Concept in Action



Visualize the addition of a chromosome that leads to Down syndrome in this [video simulation](#).

Humans display dramatic deleterious effects with autosomal trisomies and monosomies. Therefore, it may seem counterintuitive that human females and males can function normally, despite carrying different numbers of the X chromosome. In part, this occurs because of a process called **X inactivation**. Early in development, when female mammalian embryos consist of just a few thousand cells, one X chromosome in each cell inactivates by condensing into a structure called a Barr body. The genes on the inactive X chromosome are not expressed. The particular X chromosome (maternally or paternally derived) that is inactivated in each cell is random, but once the inactivation occurs, all cells descended from that cell will have the same inactive X chromosome. By this process, females compensate for their double genetic dose of X chromosome.

In so-called “tortoiseshell” cats, X inactivation is observed as coat-color variegation ([\[link\]](#)). Females heterozygous for an X-linked coat color gene will express one of two different coat colors over different regions of their body, corresponding to whichever X chromosome is inactivated in the embryonic cell progenitor of that region. When you see a tortoiseshell cat, you will know that it has to be a female.



Embryonic inactivation of
one of two different X

chromosomes encoding
different coat colors gives
rise to the tortoiseshell
phenotype in cats. (credit:
Michael Bodega)

In an individual carrying an abnormal number of X chromosomes, cellular mechanisms will inactivate all but one X in each of her cells. As a result, X-chromosomal abnormalities are typically associated with mild mental and physical defects, as well as sterility. If the X chromosome is absent altogether, the individual will not develop.

Several errors in sex chromosome number have been characterized. Individuals with three X chromosomes, called triplo-X, appear female but express developmental delays and reduced fertility. The XXY chromosome complement, corresponding to one type of Klinefelter syndrome, corresponds to male individuals with small testes, enlarged breasts, and reduced body hair. The extra X chromosome undergoes inactivation to compensate for the excess genetic dosage. Turner syndrome, characterized as an X0 chromosome complement (i.e., only a single sex chromosome), corresponds to a female individual with short stature, webbed skin in the neck region, hearing and cardiac impairments, and sterility.

An individual with more than the correct number of chromosome sets (two for diploid species) is called **polyploid**. For instance, fertilization of an abnormal diploid egg with a normal haploid sperm would yield a triploid zygote. Polyploid animals are extremely rare, with only a few examples among the flatworms, crustaceans, amphibians, fish, and lizards. Triploid animals are sterile because meiosis cannot proceed normally with an odd number of chromosome sets. In contrast, polyploidy is very common in the plant kingdom, and polyploid plants tend to be larger and more robust than euploids of their species.

Chromosome Structural Rearrangements

Cytologists have characterized numerous structural rearrangements in chromosomes, including partial duplications, deletions, inversions, and translocations. Duplications and deletions often produce offspring that survive but exhibit physical and mental abnormalities. Cri-du-chat (from the French for “cry of the cat”) is a syndrome associated with nervous system abnormalities and identifiable physical features that results from a deletion of most of the small arm of chromosome 5 ([link](#)). Infants with this genotype emit a characteristic high-pitched cry upon which the disorder’s name is based.



This individual with cri-du-chat syndrome is shown at various ages: (A) age two, (B) age four, (C) age

nine, and (D) age 12. (credit: Paola Cerruti Mainardi)

Chromosome inversions and translocations can be identified by observing cells during meiosis because homologous chromosomes with a rearrangement in one of the pair must contort to maintain appropriate gene alignment and pair effectively during prophase I.

A **chromosome inversion** is the detachment, 180° rotation, and reinsertion of part of a chromosome ([link](#)). Unless they disrupt a gene sequence, inversions only change the orientation of genes and are likely to have more mild effects than aneuploid errors.

Note:

Evolution in Action

The Chromosome 18 Inversion

Not all structural rearrangements of chromosomes produce nonviable, impaired, or infertile individuals. In rare instances, such a change can result in the evolution of a new species. In fact, an inversion in chromosome 18 appears to have contributed to the evolution of humans. This inversion is not present in our closest genetic relatives, the chimpanzees.

The chromosome 18 inversion is believed to have occurred in early humans following their divergence from a common ancestor with chimpanzees approximately five million years ago. Researchers have suggested that a long stretch of DNA was duplicated on chromosome 18 of an ancestor to humans, but that during the duplication it was inverted (inserted into the chromosome in reverse orientation).

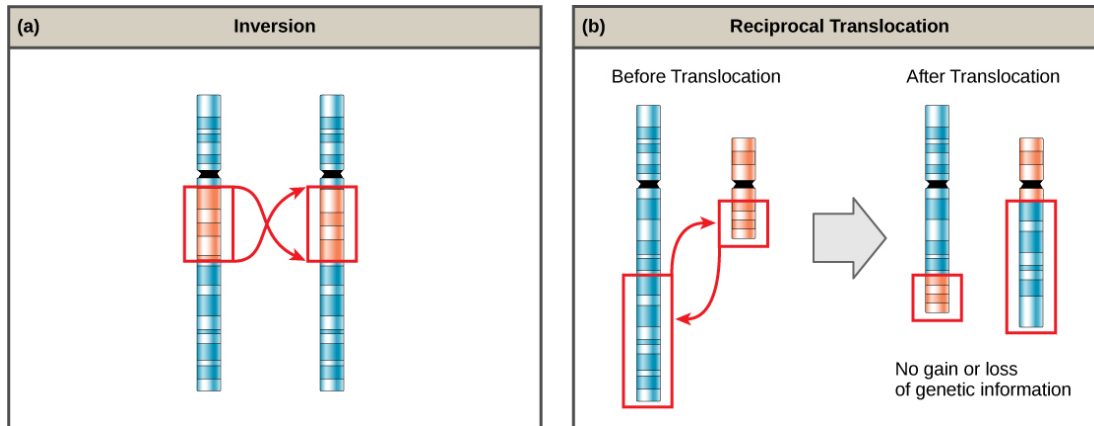
A comparison of human and chimpanzee genes in the region of this inversion indicates that two genes—*ROCK1* and *USP14*—are farther apart on human chromosome 18 than they are on the corresponding chimpanzee chromosome. This suggests that one of the inversion breakpoints occurred between these two genes. Interestingly, humans and chimpanzees express *USP14* at distinct levels in specific cell types, including cortical cells and fibroblasts. Perhaps the chromosome 18 inversion in an ancestral human

repositioned specific genes and reset their expression levels in a useful way. Because both *ROCK1* and *USP14* code for enzymes, a change in their expression could alter cellular function. It is not known how this inversion contributed to hominid evolution, but it appears to be a significant factor in the divergence of humans from other primates. [\[footnote\]](#)

V Goidts, et al., “Segmental duplication associated with the human-specific inversion of chromosome 18: a further example of the impact of segmental duplications on karyotype and genome evolution in primates,” *Human Genetics*, 115 (2004):116–22.

A translocation occurs when a segment of a chromosome dissociates and reattaches to a different, nonhomologous chromosome. Translocations can be benign or have devastating effects, depending on how the positions of genes are altered with respect to regulatory sequences. Notably, specific translocations have been associated with several cancers and with schizophrenia. Reciprocal translocations result from the exchange of chromosome segments between two nonhomologous chromosomes such that there is no gain or loss of genetic information ([\[link\]](#)).

An (a) inversion occurs when a chromosome segment breaks from the chromosome, reverses its orientation, and then reattaches in the original position. A (b) reciprocal translocation occurs between two nonhomologous chromosomes and does not cause any genetic information to be lost or duplicated. (credit: modification of work by National Human Genome Research Institute (USA))



Section Summary

The number, size, shape, and banding pattern of chromosomes make them easily identifiable in a karyogram and allow for the assessment of many chromosomal abnormalities. Disorders in chromosome number, or aneuploidies, are typically lethal to the embryo, although a few trisomic genotypes are viable. Because of X inactivation, aberrations in sex chromosomes typically have milder effects on an individual. Aneuploidies also include instances in which segments of a chromosome are duplicated or deleted. Chromosome structures also may be rearranged, for example by inversion or translocation. Both of these aberrations can result in negative effects on development, or death. Because they force chromosomes to assume contorted pairings during meiosis I, inversions and translocations are often associated with reduced fertility because of the likelihood of nondisjunction.

Multiple Choice

Exercise:

Problem: The genotype XXY corresponds to:

- a. Klinefelter syndrome
- b. Turner syndrome
- c. Triplo-X
- d. Jacob syndrome

Solution:

A

Exercise:

Problem:

Abnormalities in the number of X chromosomes tend to be milder than the same abnormalities in autosomes because of _____.

- a. deletions
- b. nonhomologous recombination
- c. synapsis
- d. X inactivation

Solution:

D

Exercise:

Problem:

Aneuploidies are deleterious for the individual because of what phenomenon?

- a. nondisjunction
- b. gene dosage
- c. meiotic errors
- d. X inactivation

Solution:

B

Free Response

Exercise:

Problem:

Individuals with trisomy 21 are more likely to survive to adulthood than individuals with trisomy 18. Based on what you know about aneuploidies from this module, what can you hypothesize about chromosomes 21 and 18?

Solution:

The problems caused by trisomies arise because the genes on the chromosome that is present in three copies produce more product than genes on chromosomes with only two copies. The cell does not have a way to adjust the amount of product, and the lack of balance causes problems in development and the maintenance of the individual. Each chromosome is different, and the differences in survivability could have to do with the numbers of genes on the two chromosomes. Chromosome 21 may be a smaller chromosome, so there are fewer unbalanced gene products. It is also possible that chromosome 21 carries genes whose products are less sensitive to differences in dosage than chromosome 18. The genes may be less involved in critical pathways, or the differences in dosage may make less of a difference to those pathways.

Glossary

aneuploid

an individual with an error in chromosome number; includes deletions and duplications of chromosome segments

autosome

any of the non-sex chromosomes

chromosome inversion

the detachment, 180° rotation, and reinsertion of a chromosome arm

euploid

an individual with the appropriate number of chromosomes for their species

karyogram

the photographic image of a karyotype

karyotype

the number and appearance of an individual's chromosomes, including the size, banding patterns, and centromere position

monosomy

an otherwise diploid genotype in which one chromosome is missing

nondisjunction

the failure of synapsed homologs to completely separate and migrate to separate poles during the first cell division of meiosis

polyploid

an individual with an incorrect number of chromosome sets

translocation

the process by which one segment of a chromosome dissociates and reattaches to a different, nonhomologous chromosome

trisomy

an otherwise diploid genotype in which one entire chromosome is duplicated

X inactivation

the condensation of X chromosomes into Barr bodies during embryonic development in females to compensate for the double genetic dose

Bis2A 16.3 Sexual Reproduction

By the end of this section, you will be able to:

- Explain that variation among offspring is a potential evolutionary advantage resulting from sexual reproduction
- Describe the three different life-cycle strategies among sexual multicellular organisms and their commonalities

Sexual reproduction was an early evolutionary innovation after the appearance of eukaryotic cells. The fact that most eukaryotes reproduce sexually is evidence of its evolutionary success. In many animals, it is the only mode of reproduction. And yet, scientists recognize some real disadvantages to sexual reproduction. On the surface, offspring that are genetically identical to the parent may appear to be more advantageous. If the parent organism is successfully occupying a habitat, offspring with the same traits would be similarly successful. There is also the obvious benefit to an organism that can produce offspring by asexual budding, fragmentation, or asexual eggs. These methods of reproduction do not require another organism of the opposite sex. There is no need to expend energy finding or attracting a mate. That energy can be spent on producing more offspring. Indeed, some organisms that lead a solitary lifestyle have retained the ability to reproduce asexually. In addition, asexual populations only have female individuals, so every individual is capable of reproduction. In contrast, the males in sexual populations (half the population) are not producing offspring themselves. Because of this, an asexual population can grow twice as fast as a sexual population in theory. This means that in competition, the asexual population would have the advantage. All of these advantages to asexual reproduction, which are also disadvantages to sexual reproduction, should mean that the number of species with asexual reproduction should be more common.

However, multicellular organisms that exclusively depend on asexual reproduction are exceedingly rare. Why is sexual reproduction so common? This is one of the important questions in biology and has been the focus of much research from the latter half of the twentieth century until now. A likely explanation is that the variation that sexual reproduction creates among offspring is very important to the survival and reproduction of those

offspring. The only source of variation in asexual organisms is mutation. This is the ultimate source of variation in sexual organisms. In addition, those different mutations are continually reshuffled from one generation to the next when different parents combine their unique genomes, and the genes are mixed into different combinations by the process of **meiosis**. Meiosis is the division of the contents of the nucleus that divides the chromosomes among gametes. Variation is introduced during meiosis, as well as when the gametes combine in fertilization.

Note:

Evolution in Action

The Red Queen Hypothesis

There is no question that sexual reproduction provides evolutionary advantages to organisms that employ this mechanism to produce offspring. The problematic question is why, even in the face of fairly stable conditions, sexual reproduction persists when it is more difficult and produces fewer offspring for individual organisms? Variation is the outcome of sexual reproduction, but why are ongoing variations necessary? Enter the Red Queen hypothesis, first proposed by Leigh Van Valen in 1973. [\[footnote\]](#) The concept was named in reference to the Red Queen's race in Lewis Carroll's book, *Through the Looking-Glass*, in which the Red Queen says one must run at full speed just to stay where one is.

Leigh Van Valen, "A new evolutionary law," *Evolutionary Theory* 1 (1973): 1–30.

All species coevolve with other organisms. For example, predators coevolve with their prey, and parasites coevolve with their hosts. A remarkable example of coevolution between predators and their prey is the unique coadaptation of night flying bats and their moth prey. Bats find their prey by emitting high-pitched clicks, but moths have evolved simple ears to hear these clicks so they can avoid the bats. The moths have also adapted behaviors, such as flying away from the bat when they first hear it, or dropping suddenly to the ground when the bat is upon them. Bats have evolved "quiet" clicks in an attempt to evade the moth's hearing. Some moths have evolved the ability to respond to the bats' clicks with their own clicks as a strategy to confuse the bats echolocation abilities.

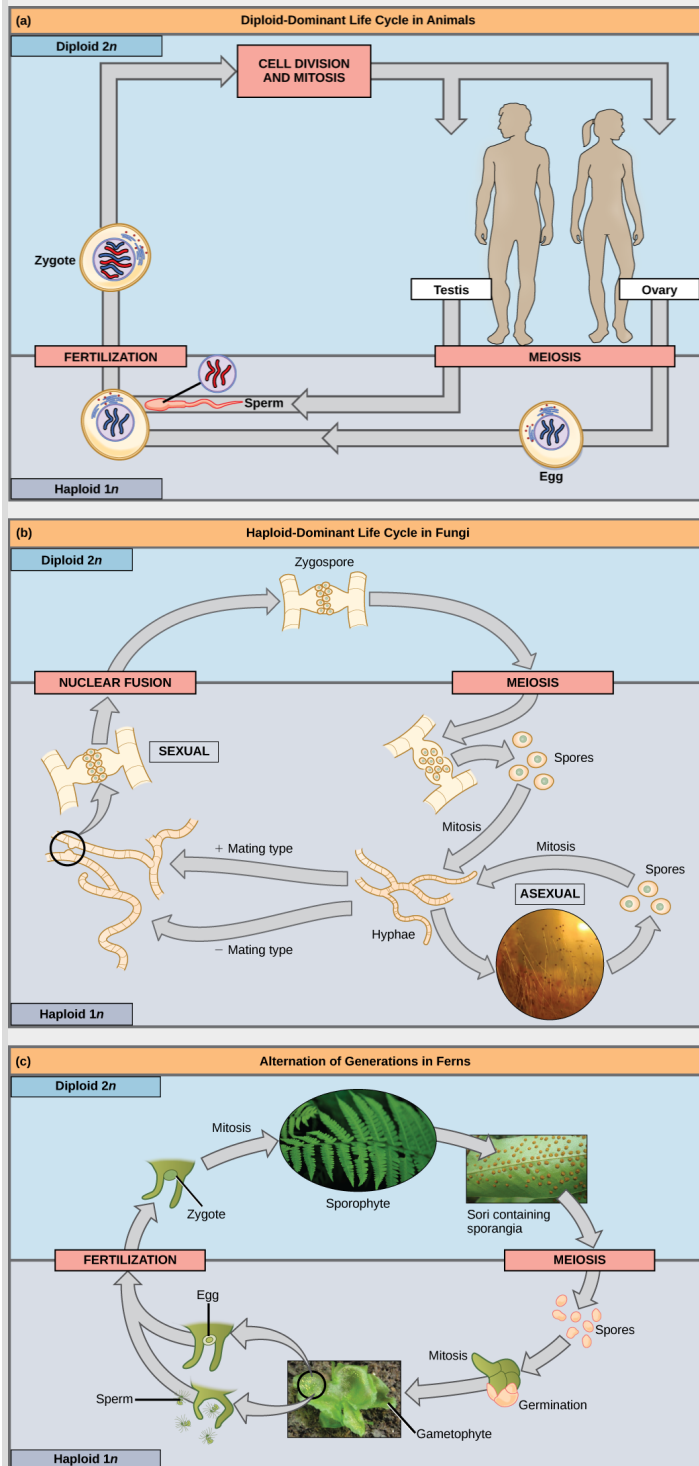
Each tiny advantage gained by favorable variation gives a species an edge over close competitors, predators, parasites, or even prey. The only method that will allow a coevolving species to keep its own share of the resources is also to continually improve its ability to survive and produce offspring. As one species gains an advantage, other species must also develop an advantage or they will be outcompeted. No single species progresses too far ahead because genetic variation among progeny of sexual reproduction provides all species with a mechanism to produce adapted individuals. Species whose individuals cannot keep up become extinct. The Red Queen's catchphrase was, "It takes all the running you can do to stay in the same place." This is an apt description of coevolution between competing species.

Life Cycles of Sexually Reproducing Organisms

Fertilization and meiosis alternate in sexual **life cycles**. What happens between these two events depends on the organism. The process of meiosis reduces the resulting gamete's chromosome number by half. Fertilization, the joining of two haploid gametes, restores the diploid condition. There are three main categories of life cycles in multicellular organisms: **diploid-dominant**, in which the multicellular diploid stage is the most obvious life stage (and there is no multicellular haploid stage), as with most animals including humans; **haploid-dominant**, in which the multicellular haploid stage is the most obvious life stage (and there is no multicellular diploid stage), as with all fungi and some algae; and **alternation of generations**, in which the two stages, haploid and diploid, are apparent to one degree or another depending on the group, as with plants and some algae.

Nearly all animals employ a diploid-dominant life-cycle strategy in which the only haploid cells produced by the organism are the gametes. The gametes are produced from diploid **germ cells**, a special cell line that only produces gametes. Once the haploid gametes are formed, they lose the ability to divide again. There is no multicellular haploid life stage. Fertilization occurs with the fusion of two gametes, usually from different individuals, restoring the diploid state ([link](#)a).

Note:
Art Connection



(a) In animals, sexually reproducing adults form haploid gametes from

diploid germ cells. (b) Fungi, such as black bread mold (*Rhizopus nigricans*), have haploid-dominant life cycles. (c) Plants have a life cycle that alternates between a multicellular haploid organism and a multicellular diploid organism. (credit c “fern”: modification of work by Cory Zanker; credit c “gametophyte”: modification of work by “Vlmastra”/Wikimedia Commons)

If a mutation occurs so that a fungus is no longer able to produce a minus mating type, will it still be able to reproduce?

Most fungi and algae employ a life-cycle strategy in which the multicellular “body” of the organism is haploid. During sexual reproduction, specialized haploid cells from two individuals join to form a diploid zygote. The zygote immediately undergoes meiosis to form four haploid cells called spores ([link](#)b).

The third life-cycle type, employed by some algae and all plants, is called alternation of generations. These species have both haploid and diploid multicellular organisms as part of their life cycle. The haploid multicellular plants are called **gametophytes** because they produce gametes. Meiosis is not involved in the production of gametes in this case, as the organism that produces gametes is already haploid. Fertilization between the gametes forms a diploid zygote. The zygote will undergo many rounds of mitosis and give rise to a diploid multicellular plant called a **sporophyte**. Specialized cells of the sporophyte will undergo meiosis and produce haploid spores. The spores will develop into the gametophytes ([link](#)c).

Section Summary

Nearly all eukaryotes undergo sexual reproduction. The variation introduced into the reproductive cells by meiosis appears to be one of the advantages of sexual reproduction that has made it so successful. Meiosis and fertilization alternate in sexual life cycles. The process of meiosis produces genetically unique reproductive cells called gametes, which have half the number of chromosomes as the parent cell. Fertilization, the fusion of haploid gametes from two individuals, restores the diploid condition. Thus, sexually reproducing organisms alternate between haploid and diploid stages. However, the ways in which reproductive cells are produced and the timing between meiosis and fertilization vary greatly. There are three main categories of life cycles: diploid-dominant, demonstrated by most animals; haploid-dominant, demonstrated by all fungi and some algae; and alternation of generations, demonstrated by plants and some algae.

Art Connections

Exercise:

Problem:

[\[link\]](#) If a mutation occurs so that a fungus is no longer able to produce a minus mating type, will it still be able to reproduce?

Solution:

[\[link\]](#) Yes, it will be able to reproduce asexually.

Multiple Choice

Exercise:

Problem:

What is a likely evolutionary advantage of sexual reproduction over asexual reproduction?

- a. sexual reproduction involves fewer steps
- b. less chance of using up the resources in a given environment

- c. sexual reproduction results in greater variation in the offspring
 - d. sexual reproduction is more cost-effective
-

Solution:

C

Exercise:

Problem:

Which type of life cycle has both a haploid and diploid multicellular stage?

- a. an asexual life cycle
 - b. diploid-dominant
 - c. haploid-dominant
 - d. alternation of generations
-

Solution:

D

Exercise:

Problem: Which event leads to a diploid cell in a life cycle?

- a. meiosis
 - b. fertilization
 - c. alternation of generations
 - d. mutation
-

Solution:

B

Free Response

Exercise:

Problem:

Explain the advantage that populations of sexually reproducing organisms have over asexually reproducing organisms?

Solution:

The offspring of sexually reproducing organisms are all genetically unique. Because of this, sexually reproducing organisms may have more successful survival of offspring in environments that change than asexually reproducing organisms, whose offspring are all genetically identical. In addition, the rate of adaptation of sexually reproducing organisms is higher, because of their increased variation. This may allow sexually reproducing organisms to adapt more quickly to competitors and parasites, who are evolving new ways to exploit or outcompete them.

Exercise:

Problem:

Describe the two events that are common to all sexually reproducing organisms and how they fit into the different life cycles of those organisms.

Solution:

The two events common to all sexually reproducing organisms are meiosis and fertilization. Meiosis reduces a diploid cell to a haploid state. The haploid cell may divide mitotically to produce an organism, some of whose cells will combine during fertilization, or the haploid cells produced by meiosis may immediately combine in fertilization to produce a diploid cell that divides to produce an organism.

Glossary

alternation of generations

a life-cycle type in which the diploid and haploid stages alternate

diploid-dominant

a life-cycle type in which the multicellular diploid stage is prevalent

haploid-dominant

a life-cycle type in which the multicellular haploid stage is prevalent

gametophyte

a multicellular haploid life-cycle stage that produces gametes

germ cell

a specialized cell that produces gametes, such as eggs or sperm

life cycle

the sequence of events in the development of an organism and the production of cells that produce offspring

meiosis

a nuclear division process that results in four haploid cells

sporophyte

a multicellular diploid life-cycle stage that produces spores